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ARCHIVES OF SURGERY

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PNEUMATIC RUPTURE OF THE INTESTINAL CANAL

WITH EXPERIMENTAL DATA SHOWING THE MECHANISM OF PERFORATION AND THE PRESSURE REQUIRED *

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BROOKLYN

Pneumatic rupture of the intestinal canal is one of the most uncommon conditions, and is due to the introduction of air under pressure into the oral cavity or the rectum.

Forty cases of pneumatic rupture of the alimentary canal, including one case of rupture of the esophagus, have been reported previously. The one reported and the three referred to in this paper increase the total to forty-four cases.

Twenty-six years ago (1904), G. W. Stone [1] of London reported the first case of pneumatic rupture of the intestine. The other cases recorded are: Andrews,[2] one, with a review of fifteen others; Bendixen and Blything,[3] one, with a collection of seven others; Fauquez [4] and Jean [5] of France, two each, and one each by Block and Weissman,[6] Buchbinder,[7] Cotton,[8] Duval [9] of France, Hailes [10] of Australia, Hays,[11]

* Submitted for publication, Aug. 16, 1930.

* From the First Surgical Service, Methodist Episcopal Hospital.

1. Stone, G. W.: Rupture of Bowel Caused by Compressed Air, Lancet **2**:216, 1904.

2. Andrews, E. Wyllys: Pneumatic Rupture of the Intestine: A New Type of Industrial Accident, Surg. Gynec. Obst. **12**:63, 1911.

3. Bendixen and Blything: Pneumatic Rupture of the Bowel, Surg. Gynec. Obst. **18**:73, 1914.

4. Fauquez: Bulletin chirurgical des accidents de travail, 1925.

5. Jean, G.: Ruptures recto-coliques produites par l'air comprime (reported with C. Lenormant), Bull. et mém. Soc. de chir. de Paris **47**:440, 1921; Ruptures recto-coliques produites par l'air comprime, Presse méd. **29**:675, 1921; abstr., J. A. M. A. **77**:1137 (Oct. 1) 1921. Lenormant, C.: Une variété d'accident du travail; Les ruptures du tube digestif produites par l'air comprime, Presse méd. **19**:486, 1911.

6. Block, F. B., and Weissman, M. I.: Pneumatic Rupture of the Sigmoid: Report of a Case, J. A. M. A. **86**:1597 (May 22) 1926.

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8. Cotton, F. J.: Rupture of the Bowel from Compressed Air, Boston M. & S. J. **166**:562, 1912.

9. Duval, P.: Bull. et mém. Soc. de chir. de Paris **47**:450, 1921.

10. Hailes, W. A.: Rupture of Bowel by Compressed Air, M. J. Australia **2**:538, 1921.

11. Hays, G. L.: Pneumatic Rupture of the Bowel, Surg. Gynec. Obst. **43**:491, 1926.

Houzel [12] of France, Morris,[13] Schwartz [14] and Sparkman.[15] Petrin [16] of Germany presented one case of rupture of the esophagus.

THE PRESSURE REQUIRED TO RUPTURE THE VARIOUS PARTS OF THE INTESTINAL TRACT

An extensive search of the original literature reveals that very little work has been done on this subject, and that few details have been presented by the investigators who have published their results. No detailed or systematic study of the pressure required to rupture the various portions of the alimentary tract has been recorded. No attempt has been made to demonstrate the mechanism of rupture, and there is presented no comparison of the relative strength of the various sections.

E. Quenu [17] of France was the first investigator to publish the results of an experiment along these lines. In 1882, in the *Revue de Chirurgie,* he described the technic for this procedure. He dissected the anus free and ligated its lower portion. Then by the use of a pressure pump he introduced air into the upper portion of the rectum, and found that the intestines would bear a pressure of from 50 to 60 cm. of mercury without rupturing. At a pressure of 70 cm. of mercury the peritoneum ruptured in several places; this was followed immediately by the rupture of the other coats. He stated that it is not reasonable to suppose that the same pressure is required to rupture the intestine within the body.

In 1911, E. Wyllys Andrews [2] of Chicago published the only other data that I have found relative to this subject. Using a pressure gage and a tank of compressed air, he did some experiments on the pressure required to rupture human, dog and ox intestines outside the body. He found this to be from 6 to 10 pounds (2.7 to 4.5 Kg.). Andrews further tested fresh specimens of the stomach, bladder and intestines from meat shops and from experiments on the dog, and never found one capable of bearing more than 12½ pounds (5.6 Kg.), most of them rupturing with a pressure of between 7 and 8 pounds (3.2 and 3.6 Kg.). He stated that Senn found that a bowel diseased with enteritis ruptured at 1½ pounds (0.7 Kg.) of pressure.

12. Houzel, G.: Rupture of Intestine by Compressed Air, Arch méd.-chir. de Province **16**:513, 1926.

13. Morris, R. B.: Pneumatic Rupture of Intestine with Roentgen Ray Studies Following Recovery: Case Report, Am. J. Roentgenol. **18**:560, 1927.

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15. Sparkman, J. R.: Unusual Case of Intestinal Rupture, J. South Carolina M. A. **18**:324, 1922.

16. Petrin, G.: Ein fall von traumatischer Oesophagusruptur, nebst bemerkungen über die Entstehung der Oesophagusrupturen, Beitr. z. klin. Chir. **61**:265, 1908.

17. Quenu, E.: Des ruptures spontanées du rectum, Rev. de chir., 1882, p. 173.

In 1921, P. Duval of France stated that he believed the dominant factor in the perforation of the intestine to be the rapidity of introduction of the air rather than the degree of pressure used. He cited one case with enormous abdominal dilatation which was shown by roentgen ray to be due to gaseous distention of the large intestine. This patient was said to present a picture typical of a total megacolon, and under this diagnosis went to the operating room, where a laparotomy showed neither a lesion nor a malformation of the colon. On further questioning of the patient after the operation, Duval learned that the patient had inflated his colon by forcing air through the anus with a bicycle pump. The pressure was not sufficiently elevated to cause a rupture of the intestine, probably because the introduction of the pressure was under the control of the patient.

In view of the marked incompleteness of information relative to the pressure required to rupture the intestines, I became interested in this problem, and performed numerous experiments on the human intestine in the autopsy room. Portions of the rectum, sigmoid, transverse colon, cecum, ileum, jejunum, stomach and esophagus have been selected. When possible the mesentery was removed with the specimens.

EQUIPMENT EMPLOYED

The equipment (fig. 1) employed for the measurement of the pressure was a manometer which I devised. It consists of a millimeter scale beside a "U" glass tube, 4 mm. in internal diameter, containing mercury, supported by a wooden upright stand, and a tank of compressed air. The pressure of the air in the tank may be at any height, so long as it is well above that at which rupture of the specimens occurs. The approximate maximum pressure in the tanks used for this experimentation was 65 pounds (29.5 Kg.) per square inch. The release apparatus was made so as to permit either a rapid or a slow exit of the confined air. To the manometer and to the tank was attached, by means of pressure rubber tubing, a curved glass tube (Paul's) so constructed that there was an elevated ridge near the end of the tube, which prevented the specimen from slipping off when it was securely fastened and pressure applied. A valve of an automobile tire was placed in the tube leading from the tank to the specimen for the purpose of maintaining the pressure in the specimen at any particular point, so that observations could be made.

APPLICATION AND RECORDING OF PRESSURE

The specimens, from 5 to 6 inches (12.5 to 15 cm.) in length, were attached by means of 2 inch (5 cm.) gauze bandage tied securely around the ends of the segments of the intestine which had been slipped over the free ends of the glass tubes, as shown in figure 1, where a portion of

transverse colon was attached to the equipment. Inflation was begun by releasing compressed air at the rate of about 2 cm. (0.38 pounds) of mercury per second. The reading of the manometer was recorded when the first rupture occurred and again when perforation of the mucosa took place, or when a simultaneous rupture of all of the layers occurred. On the manometer the reading from the starting point of the column of mercury to the point of rupture was multiplied by two in

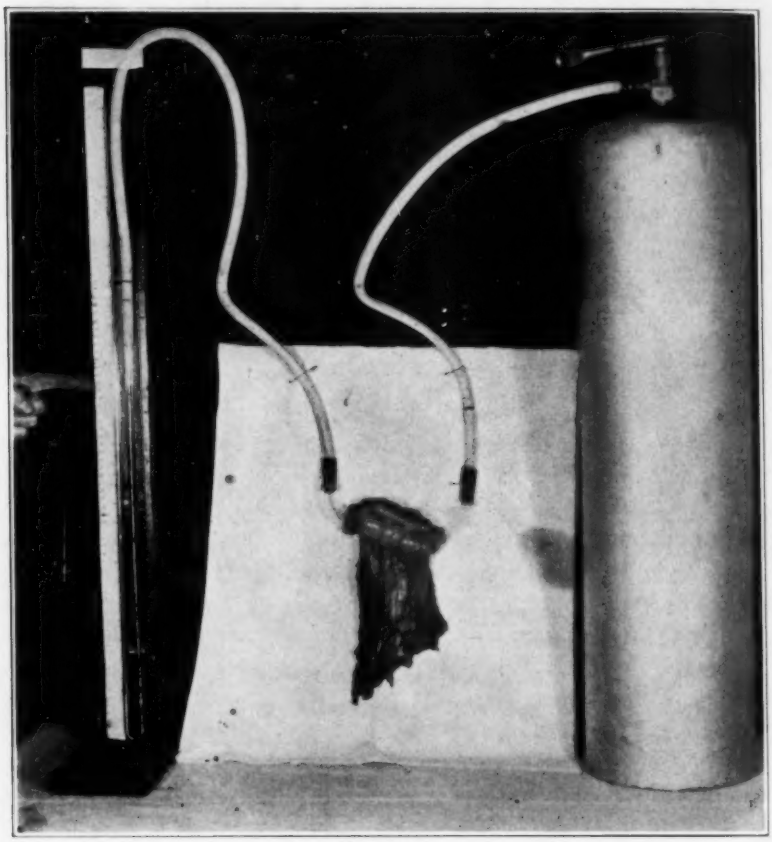

Fig. 1.—Equipment used in measuring the pressure required to rupture the intestines. The mercury manometer and tank of compressed air are connected by rubber tubes with attached Paul's tubes, and a section of transverse colon, partially inflated. The hand points to the level of the mercury in the manometer. The black line in the tube leading from the tank is where the tire valve is located.

order to obtain the pressure in centimeters of mercury at which the perforations took place. For convenience and uniformity of expression of results by observers it was necessary to convert the manometer readings into pounds per square inch. At 20 C. (average room temperature) 1 cm. of mercury is equivalent to 0.1915 pound per square inch.

When the pressure in centimeters of mercury at which the ruptures took place was multiplied by 0.1915, the pressure in pounds per square inch was obtained. These are recorded in table 1 for each specimen tested.

DATA AND THEIR COLLECTION

Data are presented in table 1 from observations on eighty-seven specimens following autopsies on seven females and eleven males, ranging in age from 5½ months to 82 years, with an average age of 42.1 years. This series includes one male child of 5½ months, one female child of 8 months and a male child of 11 years. The cause of death in each instance, the age of the patient and the particular specimens used are recorded. It will be observed that the points of rupture are not presented for many of the specimens, which is due to the fact that they were either unsuitable for testing or were discarded when the rupture did not occur entirely free from the point of attachment to the pressure equipment, thus eliminating the possibility of tearing as a result of the application of the ligature.

GENERAL OBSERVATIONS

It may be generalized from table 1 that the average pressure required to rupture the outer two coats of the various portions of the intestinal canal was 3.49 pounds per square inch, and that required to perforate the wall was 4.07 pounds per square inch. In children below 12 years of age a somewhat higher pressure was required than in the specimens from older persons. The rectum supported the greatest average pressure, and the sigmoid, ileum, esophagus, jejunum, transverse colon, cecum and stomach are in order in point of decreasing pressure required to rupture these specimens. No section was found to support a greater pressure than 11.59 pounds per square inch, which was borne by a segment of sigmoid from a child of 11 years. The greatest pressure supported by a specimen from an adult was 8.36 pounds per square inch, borne by a section of ileum.

ANATOMY

Before considering the mechanism of rupture, a brief review of the anatomy of the various portions of the alimentary canal is presented. The entire tract consists of four layers, from within outward, the mucosa, the submucosa, the muscularis, which is composed of an inner circular and an outer longitudinal layer of smooth muscle, and the serosa, except in the case of the esophagus, in which the serosa is replaced by a fibrous layer which attaches the esophagus to the surround-

ing structures. The large intestine differs from the small intestine in that the outer longitudinal layer of the muscularis of the colon is chiefly collected into three longitudinal bands of smooth muscle, which extend throughout the length of the colon. These are shorter than the inner layers, and the intestine is shortened to accommodate them, resulting in the formation of the sacculations or haustra.

TABLE 1.—*Observations on Sections from the Rectum, Sigmoid,*

Cause of Death	Sex	Age	Rectum		Sigmoid		Transverse Colon	
			Serosa	Mucosa	Serosa	Mucosa	Serosa	Mucosa
Toxic encephalitis	M	5½ mo.	10.26 AM	12.35 AM	10.64 LBL	11.78 AM	6.08 LBT	6.84 M
Upper respiratory infection; bilateral antritus.	F	8 mo.	.....	.....	5.32 LBL	11.02 AM	4.94 LBL	6.37 AM
Sinus thrombosis; postoperative pneumonia	M	11 yr.	.....	.....	10.07 LBL	11.59 AM	.....	.....
Lobar pneumonia	F	21 yr.	4.56 LBL	4.94 AM	5.32 LBL	6.08 AM	2.66 LBL	3.42 AM
Appendectomy and suspension of uterus; sudden death 12 hours ofter operation	F	30 yr.	.....	.....	2.29 LBL	5.60 AM	1.52 LBL	4.09 M
Subacute bacterial endocarditis	M	30 yr.	.....	.....	3.42 LBL	3.61 M	1.14 LBL	2.28 M
Subacute bacterial endocarditis (edema of intestines)	M	37 yr.	.....	.....	2.66 LBT	3.04 AM	.....	.....
Chronic nephritis	M	42 yr.	.....	.....	3.80 LBT	4.56 M	1.90 LBL	2.85 AM
Pyonephritis with uremia	M	42 yr.	.....	.....	2.66 LBL	2.66 M	1.90 LBL	3.04 AM
Gangrene of hand; lymphangitis and lymphadenitis	M	43 yr.	.....	.....	2.28 LBL 2.66 LBL	3.23 AM 2.66 AM	1.71 LBL	2.19 AM
Intestinal influenza	F	45 yr.	1.90 LBL	2.09 AM	2.66 LBT	2.85 AM	1.52 LBT	1.71 AM
Cirrhosis of liver; low grade peritonitis	F	50 yr.	.....	.....	2.66 LBT	3.04 AM	.....	.....
Chronic myocarditis with marked decompensation	F	60 yr.	.....	.....	2.28 LBL	3.42 AM	0.76 LBL	1.52 AM
Chronic myocarditis with slight decompensation	F	60 yr.	.....	.....	2.57 LBL	3.42 AM	1.90 LBL 1.52 LBL	2.28 AM 2.09 AM
Arteriosclerosis with cerebral thrombosis	M	62 yr.	3.04 LBL	3.42 AM	4.75 LBL	4.94 AM	1.52 LBL	2.66 AM
Bronchopneumonia	M	64 yr.	.....	.....	1.14 LBL	2.95 AM	1.71 LBL	1.81 AM
Arteriosclerosis; diabetes; chronic myocarditis	M	78 yr.	3.80 LBL	3.80 M	2.28 LBL	3.42 M	2.28 LBL	2.85 AM
Carcinoma of sigmoid; resection; local peritonitis	M	82 yr.	.....	.....	.....	.....	.....	.....
Average pressure required to rupture the various specimens in pounds per square inch			4.71	5.32	3.86	4.99	2.20	3.06

Average pressure required to rupture the outer layers of the intestinal canal is 3.49 pounds per square inch
Average pressure required to perforate the various sections of the intestinal canal is 4.07 pounds per square inch

* The figures give the pressure in pounds per square inch at which the ruptures took place in the serosa tudinal bands (LB), transversely (T) or longitudinally (L), and whether or not it took place on the mesenanterior or posterior surface (AS or PS) of the stomach. In a few of the columns the second line

MECHANISM OF RUPTURE

Large Intestine.—Gross Appearance: In the colon the ruptures took place in almost all of the specimens along one or more of the longitudinal bands at one or more points on the antimesenteric surface. The occurrence of the first rupture was generally in a longitudinal direction, though in many instances it was transversely across the muscular bands, and it involved the serosa and the muscularis. The rupture then extended along one or more of the longitudinal bands, and as the pressure was increased in the lumen of the segment, the serosa and

muscularis stripped back rapidly until a large part of the mucosa in the majority of cases was herniated through the opening in the outer two coats (fig. 2). In many instances almost all of the serosa and muscularis stripped back markedly, and the mucosa was extensively ballooned out on the antimesenteric surface. As the pressure was further increased, the herniated mucous layer perforated suddenly with a sharp,

Transverse Colon, Cecum, Ileum, Jejunum, Stomach and Esophagus *

Cecum		Ileum		Jejunum		Stomach		Esophagus	
Serosa	Mucosa	Serosa	Mucosa	Serosa	Mucosa	Serosa	Mucosa	Fibrosa	Mucosa
3.23 LBT	5.89 AM	8.74 AM	9.50 AM	7.03 M	7.03 M	3.61 LC	3.61 LC	11.02 L	11.02 L
3.04 LBL	7.22 AM	.....	.....	.....	.....	.....	.....	.....	.....
.....	.....	4.94 AM	7.60 M	4.75 M	4.75 M	1.90 LAS	1.90 LAS	8.17 L*	8.17 L
1.14 LBL	2.66 AM	8.36 M	8.36 M	4.18 M	4.18 M	2.09 LC	2.09 LC	4.56 L	4.56 L
0.76 LBL	0.95 AM	3.42 AM	3.80 AM	.....	.....	1.14 APL	2.28 LC	4.47 L	4.47 L
		1.52 AM	3.42 AM						
.....	.....	2.66 AM	2.66 AM	.....	.....	.....	.....	.....	.....
1.09 LBT	1.90 AM	3.42 AM	3.42 AM	.....	.....	.....	.....	4.94 L	4.94 L
2.09 LBL	2.85 AM	2.66 M	2.66 M	.....	.....	.....	.....	2.66 L	2.66 L
.....	.....	3.04 AM	6.08 AM	.....	.....	.....	.....	3.23 L	3.23 L
1.52 LBL	2.28 AM	5.32 M	5.32 M	.....	.....	.....	.....	.....	.....
.....	.....	5.32 AM	5.51 AM	.....	.....	.....	.....	.....	.....
.....	.....	4.37 M	4.94 M	.....	.....	.....	.....	.....	.....
1.52 LBL	1.90 AM	5.32 AM	5.32 AM	.....	.....	.....	.....	.....	.....
0.76 LBL	1.52 AM	.....	.....	.....	.....	0.38 ASGC	0.76 LC	2.42 L	2.85 L
1.14 LBL	1.90 AM	4.56 M	4.56 M	3.80 M	3.80 M	.....	.....	3.80 L	3.80 L
1.14 LBL	1.14 AM	3.04 M	3.04 M	.....	.....	.....	.....	.....	.....
0.95 LBL	1.14 AM	4.75 AM	4.75 AM	3.42 M	3.42 M	.....	.....	2.28 L	3.42 L
.....	.....	3.04 AM	3.04 AM	.....	.....	.....	.....	.....	.....
1.53	2.61	4.38	4.94	4.63	4.63	1.82	2.13	4.76	4.91

and muscularis and in the mucosa. The abbreviations indicate whether the rupture occurred along the longiteric (M) or the antimesenteric (AM) surface, or on the lesser or greater curvature (LC or GC) or on the of figures gives the pressure at which the specimens ruptured in situ.

popping sound similar to that of the bursting of a toy balloon, leaving an extensive laceration of the outer two coats and a small, ragged mucosal perforation, or the remaining tissue gradually thinned out into a fine mesh and became so thin that the air escaped through it slowly. No specimen showed more than one perforation in the mucosa.

Occasionally a rupture occurred on the mesenteric surface after the outer two coats had stripped back and left a large part of the mucosa herniated. In the mesenteric ruptures, the air dissected up the serosa for a considerable distance along the intestinal wall and around its circumference and finally caused rupture at one or more fine points

either in the mesentery proper or more commonly along the sides of the colon.

In no instance did the perforation occur on the mesenteric surface until there had been an antimesenteric rupture of the outer two coats, with herniation of the mucosa. In many instances the muscularis ruptured in several places throughout the specimen before either the mucosa or the serosa ruptured, as may be seen by the irregular distribution of these small masses of muscle between the intact inner and outer layers of the intestinal wall.

Microscopic Appearance: In order to demonstrate as nearly as possible the mechanism of rupture of the alimentary tract in the majority of cases, I have selected four microscopic sections prepared from a specimen of ascending colon ruptured at 10.53 pounds per square inch from a man of 60. It will be noted that as the pressure was applied in the specimen there was first a rupture of the serosa with slight

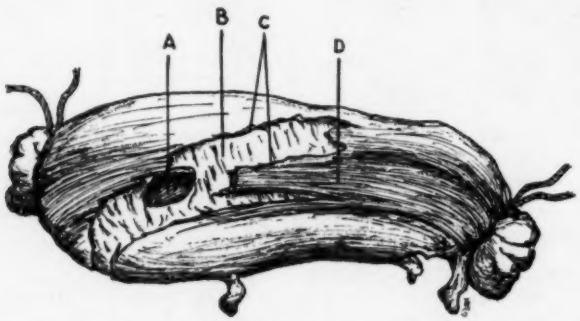

Fig. 2.—A section of colon, showing a perforation (*A*) in the mucosa (*B*), which is herniated through a laceration in the serosa and muscularis (*C*). The laceration extends principally along the longitudinal band (*D*).

separation of the underlying external muscular layer (fig. 3). The outer muscular layer was then completely lacerated, and there was a slight tear in the inner muscularis with a general separation of all of the layers (fig. 4). With further increase in pressure, the serosa stripped back, the muscular layers separated and frayed out, the submucosa was lacerated, and only the mucosa remained intact. There was a tendency to curling or rounding of the lacerated ends of the two muscular layers with the outer of these two curling over the torn ends of the inner circular fibers, indicating the tension under which the rupture took place and the tendency toward retraction of these ruptured layers. There was a noticeable appearance of general laceration and separation of all of the layers (fig. 5). A section of the edge of the perforation showed that the serosa had disappeared, the muscular layers had both retracted, and the mucosa and submucosa presented a marked wrinkling

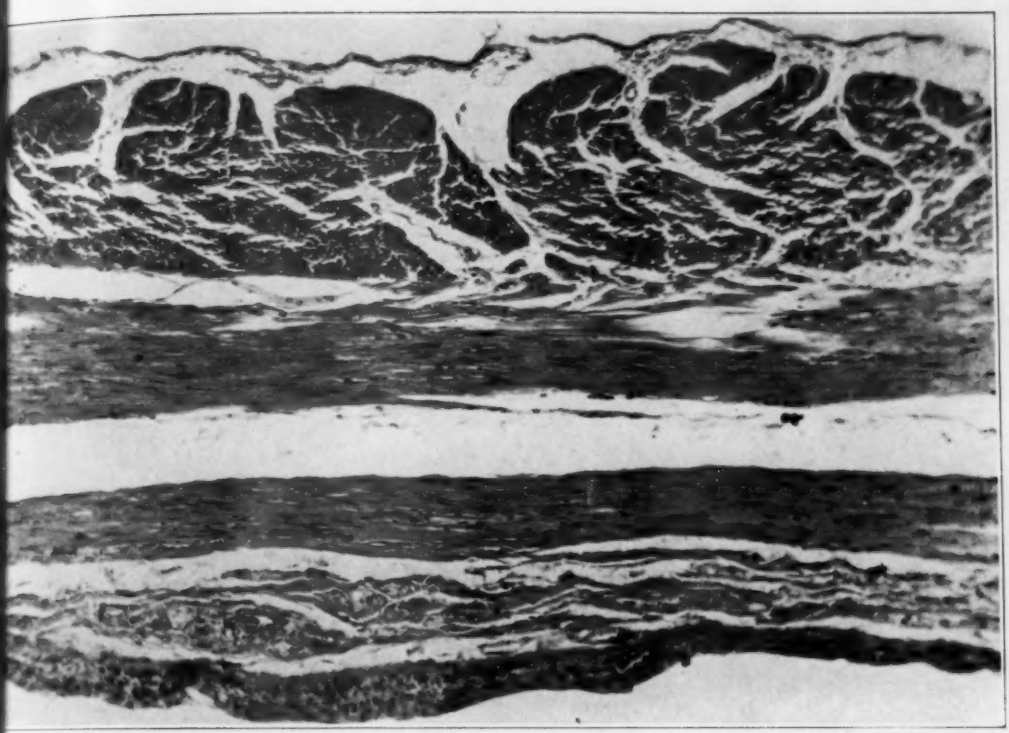

Fig. 3.—Photomicrograph of the ascending colon, showing rupture of the serosa with slight underlying laceration of the outer longitudinal muscular layer. Otherwise the section presents normal relations.

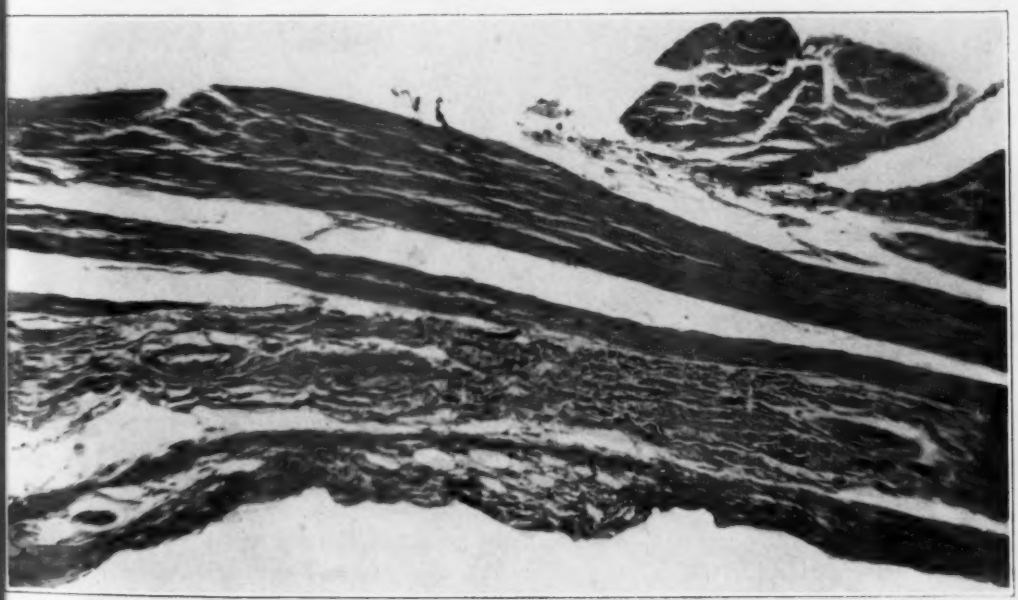

Fig. 4.—Photomicrograph of the ascending colon. Note the absence of the serosa, the complete transverse separation of the outer longitudinal muscular layer and an incomplete laceration of the inner circular muscularis.

following the rebound after the enormous distention and perforation (fig. 6).

In the meshlike lacerations and perforations of the colon, the muscular layers were markedly torn and separated, and the fibers were aggregated irregularly in small bits over the stretched mucosa. On perforation, the mucosa lost its continuity and retracted considerably, while the submucosal and subserosal connective tissue formed the larger portion of the mesh.

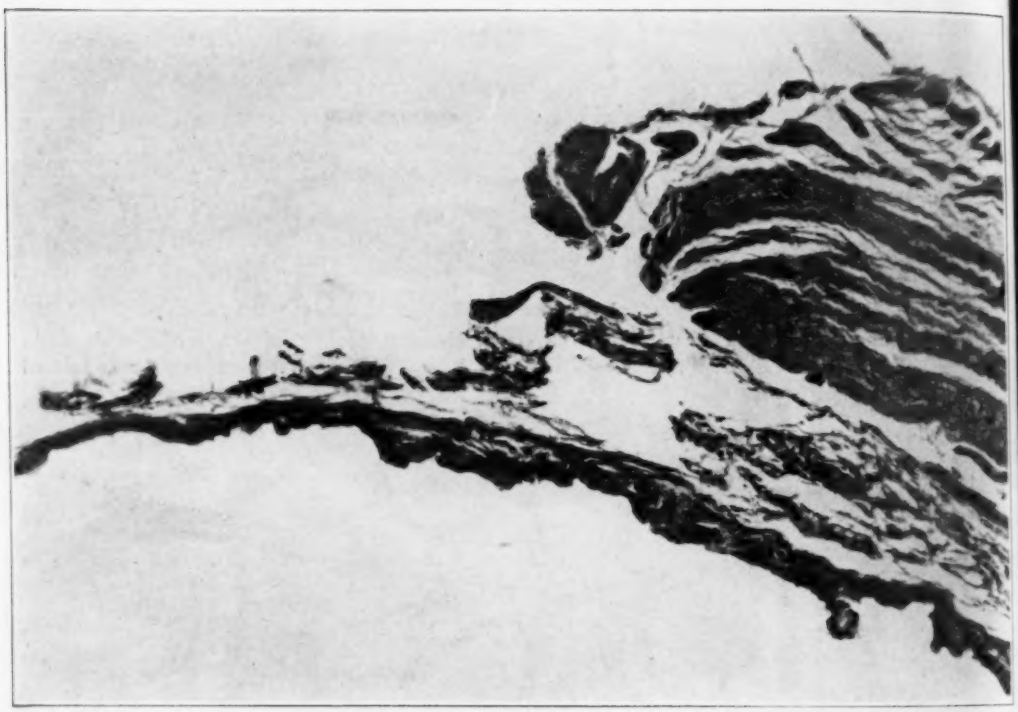

Fig. 5.—Photomicrograph of the ascending colon, presenting an absent serosa, a completely severed and frayed out muscularis, a lacerated submucosa and an intact mucosa. Note the tendency to curling of the torn ends of the muscularis, and the appearance of general laceration and separation of all of the layers.

As the mucosa was the last of the layers to rupture, in view of its greater elasticity, it would seem that it should retract more than the others, which was shown in all of the specimens after complete perforation, particularly demonstrated in figure 6.

In the specimens showing grossly a mesenteric rupture, the mesenteric and subserosal tissues showed numerous small air pockets, with a dissection of the serosa from its underlying structures.

Small Intestine.—Gross Appearance: In slightly more than half of the specimens of the small intestine the ruptures took place about the middle of the antimesenteric surface. Generally all of the layers ruptured simultaneously with much the same popping sound as in the perforation of the mucosa of the colon, leaving a small, ragged perforation of from 0.5 to 2 cm. in diameter, involving all of the layers to about the same extent. The serosa and muscularis separated and

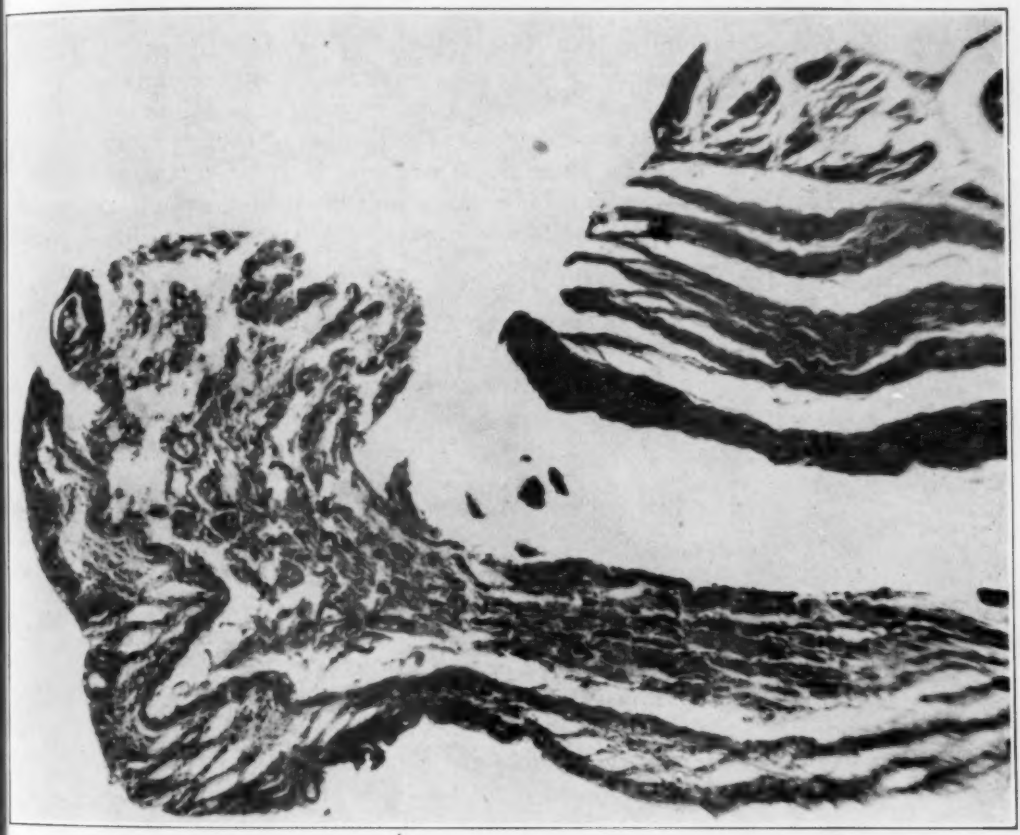

Fig. 6.—Photomicrograph of the ascending colon, showing the edge of the perforation. The mucosa and submucosa are markedly wrinkled following retraction after the enormous distention. The muscularis has separated and retracted considerably and the serosa is absent.

stripped back very little compared with the colon. In only two instances were lacerations noted in the outer two coats extending throughout most of the length of the specimens, in contrast to the usual lacerations throughout the entire length of the sections of the colon. Transversely, the edges were separated relatively slightly and thus allowed only a small

degree of herniation of the mucosa prior to the perforation (fig. 7). In the remainder of the specimens there occurred mesenteric perforations (usually from 1 to 3 cm. in diameter) in the mucosa, without any previous antimesenteric lacerations of the outer two coats. Through the perforation in the inner coat, the air escaped into the subserosal spaces and dissected up the serosa both longitudinally and circumferentially for a considerable distance, involving about one half of the circumference of the specimen, and finally ruptured through at one or more very minute points in the serosa. It was impossible to locate the points of rupture without immersing the specimens in water.

Microscopic Appearance: The small intestine (reports on sections are not included in this paper because of their similarity to the sections of the colon) showed essentially the same mechanism of rupture as was demonstrated in the large intestine. There was, however, a tendency toward less general laceration and separation of the tissues, and for all of the layers of the small intestine to rupture simultaneously, as illus-

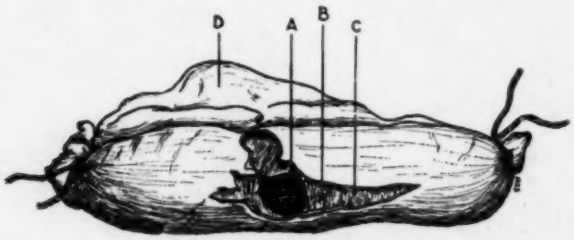

Fig. 7.—A section of ileum, presenting a perforation (*A*) in the mucosa (*B*), which is herniated slightly through a small laceration in the serosa and muscularis (*C*). The mesentery (*D*) is shown attached.

trated in figure 8. This section was taken from a gross specimen selected primarily to demonstrate the intact mucosa with a laceration of the serosa and muscularis. In addition to the typical laceration of the serosa and muscular layers, it exhibited a perforation of the mucosa just beyond the rupture of the outer two coats, thus confirming the tendency for all of the layers to rupture simultaneously.

Esophagus.—Gross Appearance: In this organ there was first a separation of the muscular layers with a relatively slight herniation of the mucosa and a rupture of the mucosa throughout almost its entire length, with a simultaneous meshlike rupture of the outer or fibrous coat, usually in such a way as to release the pressure rather slowly. Frequently, however, there was a complete perforation of all of the layers with the usual popping sound.

Microscopic Appearance: The thick muscular layers were separated and markedly retracted, while the submucosa and perieso-

phageal tissue constituted most of the remaining wall, thus indicating the greater elasticity of the connective tissue.

Stomach.—The few specimens that were tested successfully were attached to the pressure equipment at the lower end of the esophagus and at the beginning of the duodenum. These showed such irregular results that it is impossible to give any definite mechanism of the rupture of this organ.

GENERAL CONSIDERATIONS

A few specimens adjacent to the ones removed for external observations were tested in situ, and the results indicate that there is little or no difference between the pressure required to rupture the intestine in situ and that required to perforate it when removed from the body. Certainly no difference would be expected in the portions in which the

Fig. 8.—Photomicrograph of the ileum, taken primarily to show the laceration and separation of the serosa and muscularis with intact mucosa. It presents a complete laceration of the serosa and the muscularis down to the partially torn submucosa. Just to the right of the tear in the outer two layers is a perforation of the mucosa.

mesentery is long, and in which inflation would be the same inside and outside of the abdomen. There might be anticipated some difference in the cases in which the mesentery is short or absent, as in many cases of the ascending and descending colon and also in the duodenum, but no appreciable difference has been observed experimentally (table 1).

In presenting these results, I am fully aware that the pressure used and the rapidity of its application in these experiments did not simulate exactly the conditions under which the patients mentioned in the literature were injured. It was necessary to apply the pressure relatively slowly in order to observe the sequence of events in the rupture of the specimens. It was thus possible to obtain accurate information as to the

mechanism of rupture. I am also further aware that the data presented in table 1 are not sufficiently numerous to permit of conclusive observations, but they give a fair idea as to the pressure at which the various portions of the alimentary tract rupture and the manner in which the ruptures take place.

The rapidity of the introduction of the pressure is probably more important than the actual pressure itself, for it is a common experience that, roughly, the same amount of pressure applied slowly to an object without destruction will, when applied quickly, demolish that object. For example, when one throws a fragile pasteboard box with considerable force, it goes forward rapidly, but if it is struck suddenly with the same force a hole is torn in it.

TABLE 2.—*Comparison Between the Pressure at Which Perforation Took Place When the Air Was Introduced into the Intestinal Specimens Slowly and Then More Rapidly*

			Perforation Shown in Pounds per Square Inch			
			With Slow Introduction of Air		With Rapid Introduction of Air	
Sex	Age	Specimen	Number of Specimens	Average Pressure at Rupture	Number of Specimens	Average Pressure at Rupture
Male	5½ mo.	Ileum	2	8.64	6	9.46
		Jejunum	1	7.03	3	7.28
Female	21 yr.	Ileum	1	8.36	3	5.64
Male	21 yr.	Ileum	1	6.46	1	6.27
		Sigmoid	1	3.61	1	3.80
Female	79 yr.	Colon	2	2.80	5	3.32
		Ileum	2	7.22	12	5.63
		Jejunum	2	4.75	11	4.71
Average pressure at which perforation occurred when air was introduced slowly and twice as rapidly				6.26		5.87

While it is difficult to record the point of rupture of the intestine when the pressure is applied rapidly, I have endeavored to obtain some data on which a comparison may be made of the introduction of compressed air into a hollow viscus, both slowly and rapidly. The first specimen was tested in the regular manner and the result recorded. Several succeeding specimens adjacent to the first were tested with the pressure applied approximately twice as rapidly as in the first instance. The results as outlined in table 2, while meager and entirely too few from which to draw definite conclusions, are enlightening. It will be noted from table 2 that slightly less pressure is required to rupture the corresponding specimens when the pressure is introduced roughly twice as rapidly as in the first case. It is likely that there would be a still greater difference in the pressures required to rupture the intestine when the air is introduced at a relatively much greater rate, as has been almost always the case in the reports in the literature.

The question has been raised as to whether the pressure required to rupture the intestine within the intact abdomen would be the same as that necessary to rupture it outside the body. In answering this it is necessary first to consider the relative intra-abdominal and external pressure. The intra-abdominal pressure, as stated by Haven Emerson [18] in the *Archives of Internal Medicine* in 1911 and referred to by Burton-Opitz [19] in his textbook of physiology, retains a value very close to zero during quiet respirations, but, of course, the active participation of the abdominal muscles in expiration gives a much higher value. In view of this, there would seem to be very little if any difference between the pressure required to rupture the intestines inside or outside of the abdomen. Hence the average pressure of 4.07 pounds per square inch (table 1), the average found experimentally to perforate various portions of the alimentary tract outside the body, represents approximately the pressure required to rupture the intestines within the intact abdomen.

PRACTICAL APPLICATION

The practical application of these data lies in the emphasis which they tend to produce on the necessity of care in the instrumentation in the field of proctology, the intrarectal manipulation in removal of impacted feces, in the administration of the various kinds of enemas and in the handling of the intestines during surgical procedures, as it is a fairly frequent experience of the surgeon to find the intestine lacerated or ruptured when handled by unskilled persons.

With the permission of Dr. Charles H. Goodrich, the following case of pneumatic rupture of the intestine is reported from the first surgical service of the Methodist Episcopal Hospital.

CASE 1.—*History.*—J. L., a white man, aged 49, single, a shiftless laborer and a heavy drinker for years, was admitted to the Methodist Episcopal Hospital at 3:00 a. m. with a sharp, severe, epigastric pain of twelve hours' duration. His family history was irrelevant. For many years there had been a hernial protrusion in the midline of the epigastrium and one in the left inguinal region. A primary syphilitic lesion had been present twenty-two years before admission. Gonorrhea had been contracted several times. One eye had been injured and removed ten years before admission. The past history was otherwise unimportant.

The present illness began with a sudden, sharp, severe pain in the epigastrium twelve hours prior to admission, while the patient was working. He continued to work for one hour, at which time the pain became so severe that he went home to bed. Shortly afterward he vomited a small amount of greenish fluid. Following this, a dull aching sensation appeared throughout the abdomen with a persistent, severe epigastric pain. The bowels moved several times prior to the

18. Emerson, H.: Intra-Abdominal Pressures, Arch. Int. Med. **7**:754 (June) 1911.

19. Burton-Opitz, R.: Text Book of Physiology, Philadelphia, W. B. Saunders Company, 1920.

onset of pain and a short time thereafter. He vomited several times during the twelve hours prior to admission. Anorexia was pronounced after the onset of pain.

About the time the epigastric pain began, the patient noticed that the protrusion in the upper part of the abdomen had increased in size, had become quite tense and was very tender. The left inguinal region had also become prominent. This was the history elicited before the operation. The next day, twelve hours after operation, the following additional history was obtained. While at work, the patient, desiring an enema, inserted a tube into his rectum. By mistake he turned on compressed air, and immediately experienced the pain described. The abdomen became large and breathing difficult.

Examination.—On admission physical examination revealed a very muscular man, conscious, lying uneasily in bed, with marked pallor, pinched facies and anxious expression, slight cyanosis of the lips and finger-nails, cold and clammy skin and an alcoholic odor to the breath. He was evidently suffering from great pain. Respirations were grunting, at a rate of 26, and were chiefly costal. There were no abnormal pulmonary observations. The heart was slightly enlarged to percussion, and there was a blowing systolic murmur at the third left interspace. The sounds were of poor quality, somewhat irregular and at a rate of 90. The temperature by mouth was 100 F. The abdomen was greatly distended, moved only slightly with respiration and was extremely tense, and the umbilicus was almost obliterated. There was marked tympany throughout. There was no evidence of intra-abdominal fluid or of subcutaneous emphysema. About midway between the ensiform process and the umbilicus was a rounded, slightly bluish, nonreducible, tender protrusion the size of a lemon. The left inguinal ring was considerably enlarged, and through it protruded a nontender reducible mass of intestines. Rectal examination revealed considerable tenderness throughout. There was some fecal matter but no blood in the rectum. There were extensive scars over the shaft of the left tibia, a large one in the inguinal region and a small one on the glans penis. Otherwise the physical examination was negative. On admission, the leukocyte count was 11,600, 84 per cent polymorphonuclears and 16 per cent small mononuclears.

Operation.—On the basis of the preoperative history and the elicited clinical signs, a diagnosis of strangulated epigastric hernia was made, for which an operation was begun thirteen hours and fifty minutes after the injury. The anesthesia was induced with nitrous oxide and oxygen and continued with ether. The operation consumed one hour.

A transverse incision was made in the epigastrium over the hernial mass. When the peritoneum was incised, a considerable quantity of gas with a fecal odor escaped with a whistling sound. The respiratory embarrassment and the cyanosis were immediately diminished. The abdomen became much less distended and the epigastric mass much smaller. Only a small portion of the greater omentum was found to be contained in the hernial sac. The neck of the sac, which was about 1.5 cm. in diameter, was enlarged, and the omentum was released. It was found not to be strangulated. At once it was apparent that the patient's symptoms and signs were not due to a strangulated epigastric hernia. The original incision was enlarged to about 17 cm. in length and a longitudinal incision 12 cm. in length was made from the center of the first, forming a "T."

The abdomen was explored. The serosa of the colon and small intestines was greatly injected, and there was a small quantity of blood-stained fluid containing fecal particles in the pelvis. No free blood was found. The left inguinal

canal was enlarged, but did not contain any omentum or intestines. The sigmoid flexure and the lower portion of the descending colon were brought into the incision and were found to be collapsed. Beginning in the upper portion of the rectum and extending through the sigmoid flexure and the descending colon, there was marked, fresh, diffuse, subserosal hemorrhage, most extensive in the mesentery and in the mesenteric surface of the colon and rectum, though extending well around onto the antimesenteric surface. The appendices epiploicae were also markedly hemorrhagic. There were numerous small scars throughout the sigmoid. Near the junction of the sigmoid flexure with the descending colon, on the antimesenteric surface, there were two longitudinal lacerations in the serosa and muscularis, measuring 2 and 5 cm. in length and about 1 and 1.5 cm. in width. The larger of these was sutured with continuous plain catgut.

The extensive hemorrhage and the laceration of the wall suggested the previous introduction of compressed air into the rectum. In view of the presence of fecal particles and much gas in the abdominal cavity, we felt certain that a perforation of the intestine had occurred, though none could be found after several minutes of searching. A rubber drainage tube was inserted in the lower angle of the incision and a cigaret drain was placed in the pelvis through a stab wound in the midhypogastrium. The abdomen was closed in layers with silk-worm gut reinforcement.

Course.—At the close of the operation the general condition of the patient was poor. Abdominal distention and vomiting of dark brown fluid gradually increased from the second day. No peristaltic waves were audible, and no passage of fecal matter occurred through a rectal tube. Bronchopneumonia developed on the seventh day. From the third day, there was fecal discharge from the incision and increasing dehiscence of the wound with some eventration of the underlying viscera. The rectal temperature ranged between 102 and 103 F.; the pulse rate was 100, and the respiratory rate varied from 25 to 30. Gastric lavage was performed several times in the first few days, and the depletion of fluid was cared for by hypodermoclysis. Sufficient morphia was given for relief from pain, usually two doses of one-fourth grain (0.016 Gm.) in twenty-four hours. After operation the blood cells, blood chemistry and urine showed no appreciable deviation from the normal. The Wassermann reaction of the blood was negative. The blood pressure was 103 systolic and 68 diastolic. The patient's mentality remained clear, except for occasional flighty intervals, until shortly before death at 3:40 a. m. on the eighth postoperative day.

Autopsy.—An autopsy was performed, and the pathologist reported: All of the viscera of the abdomen were markedly matted together, and to the diaphragm and the lining of the abdominal cavity by a diffuse fibrinopurulent exudate, and there was a large quantity of thick, yellow pus in the pelvis and other recesses of the abdomen. Underneath the hypogastric stab wound was a ragged, gaping opening 2 inches long in the convexity of the sigmoid near its junction with the descending colon, which communicated with the abdominal cavity and contained a mass of hardened feces. This opening was just adjacent to a short line of suture in the sigmoid. The rectum, sigmoid and descending colon showed numerous white, scarred areas scattered over their surfaces, and these portions of the colon, including the appendices epiploicae together with the mesentery, were markedly hemorrhagic. There was a left inguinal hernia, the sac of which measured 6 by 4 cm. The lungs were congested and nodular, suggestive of bronchopneumonia. The heart showed nothing abnormal. The liver, spleen and pancreas were much enlarged. The prostate contained small cavities, indicative of an old prostatic abscess.

Microscopically, sections of the lower lobes of both lungs showed areas in which the alveoli were filled with desquamated epithelium, pus cells and blood; the tubules of the kidneys showed some granular degeneration, and the liver presented granular degeneration and some fatty infiltration. Otherwise, the organs showed nothing of interest.

Diagnosis.—The diagnosis was traumatic rupture of the sigmoid, general peritonitis, bronchopneumonia, chronic prostatitis and probably old syphilis.

This case is unique in that the pneumatic rupture of the intestine was associated with an epigastric and an inguinal hernia. The patient is the oldest (49 years) on record as having received this injury; the pressure of 2 pounds is the lowest so far reported as having caused this condition, and the patient is the first to give a history of this peculiar type of self-inflicted injury, not purely accidental. The patient mentioned by Duval, in 1921, was the first reported as having received an entirely intentional injury.

Dr. Loyal A. Shoudy,[20] chief surgeon for the Bethlehem Steel Company, permitted me to present the following data on three cases of pneumatic rupture of the intestines which occurred in their plants.

1. A. S., in the Elizabeth, N. J., plant, was using an air hose to dust off his clothing, when J. K., offering to help him, jokingly stuck the hose in the region of his fellow worker's rectum. A. S. fell in a faint and was rushed to the hospital, where Dr. McCallion operated and found many ruptures of the intestines. The patient recovered (July 28, 1927).

2. An accident occurred in the Bethlehem plant in 1916. A workman, in fooling, placed an air hose near the rectum of a fellow worker (S. V.). The patient died the same day.

3. St. Lukes Hospital, Bethlehem, Pa., has a record (1927) of a worker who placed an air hose near the rectum of a fellow worker. The patient was operated on by Dr. W. P. Walker and recovered.

Dr. John J. Moorehead, director of the department of traumatic surgery, New York Post-Graduate Medical School and Hospital, New York, has given me permission to report the following case (which is not included in the statistics):

Case 2.—*History.*—P. M., a white man, aged 37, an Austrian, a repairman, was admitted to the hospital at 10:40 a. m. on March 18, 1928, complaining of pain in the abdomen and right shoulder of twenty-three hours' duration. On the day before admission, while the patient was bending over washing his face and hands at his place of work, a fellow employee jokingly placed the nozzle of a compressed air line, used to clean motors, against the clothing covering the patient's anus. The nozzle was held there for only a second. The air line was connected to two pumps, though the patient did not know the amount of pressure applied to his rectum. He felt a severe, sudden pain in the rectum and the lower part of the abdomen, became dizzy and fell to the floor. He vomited once after the ingestion of magnesia three hours after the accident. He took nothing else by mouth after the accident, though he had two bowel movements, which contained no blood. He voided once in the morning prior to admission, but no blood was seen in the urine.

20. Shoudy, L. A.: Personal communication to the author.

Examination.—On admission, examination showed the patient to be in a moderate degree of shock, pale and slightly restless; the heart and lungs were surgically competent; the abdomen was distended, round and markedly tender, with the maximum tenderness in the left lower quadrant; light percussion was painful; liver dulness was obliterated, and there were signs of free fluid in the flanks.

A blood count taken before the operation showed 17,000 leukocytes, with 89 per cent polymorphonuclears.

Operation.—A diagnosis of perforation of the intestine was made, and twenty-five hours after the injury Dr. Moorehead began an operation for relief from this condition. Through an incision in the right upper quadrant, the hepatic flexure of the colon was sutured to the peritoneum preparatory to establishing a subsequent colostomy, if necessary, but no opening was made into the colon. This incision was closed with a rubber tube drain in the wound. Through an incision in the left lower quadrant, the sigmoid was found to contain three perforations, which were debrided. The larger of these was sutured and the others were left open. An iodoform gauze drain was inserted in the site of the perforations.

Course.—The postoperative temperature and pulse reactions were slight, and on the sixth day the bowels began to move through normal channels. The patient was discharged on the forty-fifth postoperative day in excellent general condition, with the abdominal wounds practically healed.

On June 19, 1930, two years after the patient was injured, he was readmitted to the Post-Graduate Hospital. For the first six months after his discharge, he felt only fairly well. He stated that during the preceding eighteen months he had grown somewhat weaker and had experienced general abdominal discomfort, which was exaggerated by exercise and the ingestion of food. He said further that he had taken only liquid food during the previous year, and that his stools had been loose and tarry, and had contained red blood since his discharge; his appetite had been poor, and he had felt some pain in his back, neck and extremities.

On readmission, physical examination gave essentially negative results. He appeared to be in excellent general condition. The blood count showed: red cells, 4,310,000; hemoglobin, 82 per cent; leukocytes, 7,600, and polymorphonuclears, 63 per cent.

Sigmoidoscopy and proctoscopy revealed some evidence of perisigmoidal adhesions or angulation of the sigmoid. There was catarrhal proctitis with some mucus that extended well up into the sigmoid. Two ulcerative areas were present on the posterior anal wall.

At the end of twenty-four hours a gastro-intestinal series of roentgenograms showed a normal distribution of the meal, though the transverse and distal colon was narrow and spastic. The distribution in the distal colon was too irregular to permit a morphologic study. No evidence of obstruction was seen.

A barium colon enema showed moderate spasm at the junction of the descending colon and sigmoid. An S-shaped loop was noted at the colonic sigmoidal junction. There was no evidence of obstruction.

This patient's subjective complaints could not be verified by the objective observations. During his ten days in the hospital he ate a regular diet, his bowels were constipated, with no blood in the movements, he did not vomit, and he had no definite complaints. He had always been considered unstable mentally and emotionally and usually had borne the brunt of the jokes of his fellow workers. It was felt definitely that he was suffering from a marked neurosis and "compensitis." Though he was discharged in excellent general condition after an extensive study, every effort to return him to his work proved futile.

ETIOLOGY

The cause of this accident is the introduction of air under pressure into the oral cavity or the anus. Compressed air is used in the operation of pneumatic hammers and drills, dusting of machinery and barrels and in many other forms of commercial art. Unfortunately some of the workers, not realizing the devastating effect of the air, in a mood of joviality, direct the end of the nozzle toward the anus of a fellow worker. It is these practical jokers who have accounted for almost all of the injuries.

There are only four of the forty cases reported that I feel fairly certain were not the results of practical jokes. In the case herein reported, the patient himself introduced the nozzle into his rectum and turned on compressed air instead of water. The patient described by Jean was injured as a result of the explosion near the anus of a tube conveying compressed air. Petrin presented a case in which the esophagus was ruptured as a consequence of the worker falling while he carried a compressed air hose in his mouth, allowing the end of the hose to be released and the air to enter the oral cavity. In the case mentioned by Duval, the patient inflated his own rectum with a bicycle pump.

Generally, one or more layers of clothing were interposed between the nozzle and the anus, but this did not reduce the great power of penetration and deadly effect of the air to any appreciable extent. The nozzle was usually several inches from the anus, though in a few instances it was tightly pressed against the anus, and was said to be introduced into the rectum in four cases. In the first of these Stone suggested that in his patient the nozzle was introduced through the anal orifice, because the injuries to the bowel were such as to lead him to think, on account of the number and size of the rents, that the intestine had been nipped between the nozzle and the sacrum, though the latter showed no sign of injury. One case presented by Andrews, another by Duval and the one herein reported are the only others in which the nozzle was said to be introduced into the rectum.

In 1911, Andrews presented the most concise and logical explanation of the gross mechanics of this injury as follows:

> I feel sure that at 50 to 125 pounds of pressure, a gas would form a column several inches in advance of the tube, and would act almost like a solid body in forcing open the sphincter. The jet of a fountain can be made to support a good size ball of some weight, so the jet of air is more than ample to force open the levator and sphincter ani muscles and the soft pelvic floor. The nates and the pelvic floor form a funnel whose apex is the anus. All confined air expanding in this funnel will force open the gut without having the end of the pipe adjusted to the anus. With the voluntary contraction of the levator ani muscles, the space between the buttocks would be narrowed and the funnel deepened, thus confining the air laterally and leading it more quickly into the bowel.

The effect of the introduction of air would be greater with the patient in a stooping attitude, a sitting posture, and when he is taken by surprise, at which time the sphincter would be most relaxed and the intra-abdominal pressure at its lowest, thus reducing the safeguard to a minimum in preventing the introduction of a foreign substance through the anal orifice.

Gant [21] stated that the bowel has been ruptured several times by ignorant and careless physicians attempting to use pneumatic sigmoidoscopes. They have overdistended the intestine with the air or have forcibly pushed the instrument through the wall of the intestine.

MORBID ANATOMY

The pathologic changes found will depend on the pressure applied, its proximity and angle of application, the individual resistance of the tissues, the contents of the bowel and numerous other minor considerations. In general, the changes may be divided into external and internal or those found at operation or necropsy.

External Changes.—Two cases reported by Andrews in which autopsies were performed showed bruises about the anus. Another case (Bendixen and Blything) showed the tissues about the anus ecchymosed and the anal sphincter stretched so as to admit four fingers. Sparkman and Schwartz each reported a case in which there was bloody mucus on the rectal tube on withdrawal. Several writers have reported prominence of the inguinal canals. Subcutaneous emphysema was noted in seven cases. In general it was confined to the trunk. One of Jean's and another of Buchbinder's also showed the external genitals involved, and in the latter case the perineum was affected. In Hailes' case it extended from the eyebrows and lower part of the scalp down over the body to Poupart's ligaments, distorting the face and interfering considerably with the proper examination of the abdomen and chest. In Petrin's case, the emphysema extended over the chest down to the navel and on the arms almost to the elbows, and was found in the mediastinal tissues.

Changes Found at Operation and Necropsy.—When the peritoneum is entered, there is generally an escape of considerable gas with a fecal odor. If there is no perforation of the intestine, the intestine is distended and there is no escape of gas on incision of the peritoneum. If it has been perforated, the intestine is generally collapsed.

Air has been found in the peritoneal cavity in several instances when no perforation could be located. This may be explained on the basis of observations which I have made on cadavers as a result of

21. Gant, S. G.: Diseases of the Rectum, Anus and Colon, Philadelphia, W. B. Saunders Company, 1923, vol. 2, p. 464.

distention of various portions of the intestines by air. When the intestine ruptured on the mesenteric surface, the air gradually elevated the serosa for a considerable distance along the intestinal wall, both longitudinally and circumferentially, and finally broke through this thin layer of tissue at one or more very minute points, thus allowing the air to escape into the general abdominal cavity and leave no macroscopic evidence of its entry. Invariably in these cases it was necessary to immerse the specimen in a basin of water to locate the points of rupture.

Moynihan [22] stated that "one sign alone is characteristic of the lesions of those portions of the bowel which are not wholly covered by peritoneum (parts of the duodenum and ascending and descending colon)—that is, emphysema." The appearance of the subcutaneous emphysema, as noted in several cases clinically, probably can be explained on the basis of my observations. Following the mesenteric rupture of the intestine, it is probable that the air dissects its way through the muscles and fascia without perforation of the serosa and enters the subcutaneous spaces to produce the clinical entity emphysema.

The rectum, various portions of the colon, the ileum, the mesosigmoid and the mesentery of the ileum and the esophagus have been reported ruptured. In all of these cases, except that mentioned by Duval, in which operation or autopsy was performed, the distention resulting from the introduction of air into the intestinal canal was sufficient to produce lacerations of the outer coats and in many instances perforation of the mucosa.

The sigmoid flexure is by far the most frequently ruptured, which is explained by the fact that it forms the first barrier to the inrushing air. It is attached by a rather long mesentery in contrast to the short or absent mesentery of the descending colon, and forms a somewhat semicircular trap for the entering air, which, similar to a solid body, tends to maintain its velocity forward in a straight line. The air thus comes in forcible contact with the sigmoidal wall where the latter tends to form almost a right angle juncture with the descending colon, when pressure is applied within its lumen.

The perforations noted clinically usually have been single, though a few have been multiple, and they have varied in size from one that was scarcely visible to one 6 inches (15.24 cm.) in diameter, as noted by Bendixen and Blything. The lacerations of the serosa and muscularis usually have been multiple and extensive, due to the fact that it is the outer coats that rupture first during the distention, thus allowing the mucosa to herniate through and eventually perforate at a higher pressure

22. Moynihan, B.: Abdominal Operations, Philadelphia, W. B. Saunders Company, 1914, vol. 2, p. 80.

than is required to tear the serosa or muscularis. Several observers have noted these lacerations and perforations to be chiefly along the longitudinal bands on the antimesenteric surface of the colon.

Andrews reported one case in which the patient died of general peritonitis, in which there was a rupture of all of the layers of the colon, except the mucosa, from the rectum to the appendix. In one case Bendixen and Blything observed extensive lacerations of the sigmoid (7 inches [17.78 cm.]), the descending and ascending colon, the mesentery of the ileum and of the ileum itself, and a 6 inch perforation near the hepatic flexure. A perforation at the base of the cecum was reported by Cotton. One case (Hailes) presented a superficial laceration of the lower end of the colon, a 3.7 cm. tear in the hepatic flexure, a markedly hemorrhagic colon, a collapsed right lung and bloody fluid in the right pleural cavity. Petrin's case presented a 6 inch longitudinal rupture of all of the coats of the esophagus with emphysema of the mediastinal tissues. Hemorrhage and ecchymoses are to be expected wherever there is damage to the intestinal wall. Several cases, particularly Hailes', Schwartz', Andrews' and mine have presented marked, diffuse, subserosal hemorrhages, most extensive in the mesentery and mesenteric surface and extending well around onto the antimesenteric surface of the colon and involving the appendices epiploicae. Duval reported a case in which the patient had markedly inflated his colon with air by using a bicycle pump. No laceration of the wall of the intestine could be located at operation, which was performed under the provisional diagnosis of total megacolon.

POSTOPERATIVE COMPLICATIONS

These complications have been mentioned particularly in only three instances, and it is interesting to note that these three patients recovered.

Andrews reported a case in which Fletcher repaired an extensive laceration of the sigmoid, which later caused intestinal obstruction due to a narrowing, for which a colostomy was performed with a subsequent resection of the constricted portion. A ventral incisional hernia was repaired.

In their case Block and Weissman reported the suturing of extensive lacerations and a perforation in the upper part of the rectum and lower end of the sigmoid and the performance of a jejunostomy. Acute intestinal obstruction developed as a result of the constriction of the injured area, for which an entero-enterostomy was performed. Acute epididymitis developed, from which the patient recovered.

Hays' case presented extensive lacerations of the upper part of the rectum and lower end of the sigmoid and a perforation of the lower end of the sigmoid, which were repaired, and the sigmoid was sutured to

the anterior peritoneum preparatory to a colostomy, which was performed on the first postoperative day because of distention, which increased to such an extent that a cecostomy was done on the second day after the operation. Drainage through the cecostomy became so free that it was evident that the patient would expire if something was not done to stop the rapid passage of fluid through this opening. The Barnes dilator was employed successfully to stop the drainage of fluid, and the patient improved markedly and recovered. Hernias developed in the abdominal incisions and were subsequently repaired, as was also the incision for the cecostomy.

ROENTGENOLOGY

A roentgenographic study was made by Morris five months after an operation on a patient showing an uneventful recovery and excellent health in the interim. This patient presented extensive lacerations of the serosa and muscular coats of the cecum, ascending colon and the sigmoid flexure, and a large quantity of blood in the pelvis and among the coils of intestines. A six hour examination showed a poor filling of the cecum and ascending colon. The contour was irregular and deformed. There were evidently numerous adhesions in the vicinity of the cecum and ascending colon. The sigmoid appeared to be normal except for a narrowing in the first portion. No other cases except Dr. Moorehead's incorporated here, have been reported as having been studied by the roentgen ray.

SYMPTOMS AND SIGNS

The symptoms and signs, though dependent on the degree of injury, are essentially the same for all cases, and may be appropriately divided into those of a local and those of a general nature.

Local (Abdominal) Symptoms.—There is usually a sudden onset of a constant, sometimes colicky, very severe pain in the lower part of the abdomen, which the patient may be unable to localize more concisely. He complains of great difficulty in breathing. The most marked feature of this condition is the enormous distention of the abdomen, which extends into the flanks, with obliteration of abdominal dulness. There is marked hyperresonance. The umbilical depression is greatly diminished or absent, and the inguinal canals are often prominent. The abdomen is rigid and tender throughout, with a maximum over the injured viscus. If the patient is seen within a very few hours after the accident, palpation of the abdomen does not produce the sensation of a diffuse peritonitis, but this may be superimposed several hours after the injury.

General Symptoms.—The patient generally shows a marked degree of shock, the skin is cold and clammy, he is usually conscious, though

many times unconscious, and his facies is pinched and presents an anxious expression. A moderate or marked degree of cyanosis and nausea and vomiting are usually present. The thighs are flexed on the abdomen. The respirations are rapid (average of 35 in the eight cases in which the rate was given), labored, grunting and costal, as a result of pressure on the diaphragm. The heart sounds and the pulse rate are accelerated and of poor quality. The rate averaged 119 in the eleven cases in which the pulse was stated to range from 74 to 190. The temperature is usually subnormal, except in cases of several hours' duration, in which peritonitis has manifested itself. Two cases of twelve and eighteen hours' duration prior to operation showed temperatures of 100 and 102 F.

Buchbinder's case manifested clonic spasms of the muscles of the trunk. Subcutaneous emphysema was noted in seven cases, and was confined chiefly to the trunk.

DIAGNOSIS

With or without a history of the introduction of compressed air into the rectum, one should be able to make a diagnosis of this condition. In a case complicated by an associated hernia the diagnosis is made more difficult. If the patient shows severe shock, cyanosis or pallor, great respiratory embarrassment, rapid and thready pulse, marked distention, hyperresonance and extreme tenderness of the abdomen, with obliteration of the umbilical depression and abdominal dulness, especially when this is found unassociated with a hernial mass, one should be able to make the correct diagnosis. With the history of the introduction of compressed air into the rectum, the diagnosis should be evident. If this history is unavailable and the surgeon is unwilling to make a definite diagnosis, he should at least label it an "acute abdominal condition" and proceed immediately with a laparotomy, provided the condition of the patient permits operative intervention.

This condition, however, must be differentiated from other acute abdominal conditions, and among the more important of these, one must consider: general peritonitis, volvulus, intussusception, ileus with or without perforation, ruptured gastric, duodenal or typhoidal ulcer, strangulated hernia, stab wound, gunshot or other traumatic perforations and ruptured lung and fractured rib with the presence of subcutaneous emphysema.

MORTALITY

The general mortality in this series of forty-four cases is 56.81 per cent. The ages in this series, as stated in twenty-nine, ranged from 13.5 to 49 years, averaging 23.8 years, with only six patients 35 or more years of age. The operative mortality is 44.82 per cent (twenty-nine patients were operated on, with sixteen recoveries and thirteen

deaths). Of the operative recoveries, the time elapsing between the occurrence of the injury and the institution of operative proceedings, as stated in eight of the fifteen cases, ranged from one hour and fifty minutes to five and one-half hours, and their ages were from 14 to 45 years, with six not given, making an average of 27.6 years. Relative to the operative deaths, ranging from 13.5 to 49 years, with an average of 23.7 years, with four not given, the time after injury that operation was begun, as stated in seven of the twelve cases, ranged from about three hours in Stone's case, in which only a paracentesis abdominis was performed ante mortem, to four days, in one of the cases reported by Bendixen and Blything, in which the patient was brought to the operating room in a moribund condition.

The nonoperative mortality is 80 per cent (of fifteen patients not operated on, twelve died). The ages of those who died after operation ranged from 16 to 27 years, with the ages of four of the twelve not given, making an average of 21.3 years. The three cases in which the patients recovered without operation were: One reported by Andrews with the age not given, in which live steam was introduced into the rectum; that of a boy, 16 years of age, mentioned by Bendixen and Blything, who recovered and returned to work shortly after the accident, and another recorded by Fauquez, in which a boy of 15 suffered from distention of the colon but recovered in a few days. The symptoms and signs in these cases were said to be such as to warrant a clinical diagnosis of rupture of the bowel.

Of the seven cases in this series showing subcutaneous emphysema, the mortality is 57 per cent.

PROGNOSIS

The prognosis is grave with or without operative intervention, but the outlook is distinctly better when an operation is performed. The results herein recorded suggest that if a patient is operated on within six hours after the injury, his chances of recovery are considerably better than if a greater time is allowed to elapse. Age seems to exert no particular influence on the results. It is of interest to observe that this condition is one of late adolescence and early adult life, the average age of the patients being 23.8 years.

TREATMENT

Operative Treatment.—The treatment "par excellence" for the abdominal condition is immediate operation, provided the general condition of the patient will permit. An intraspinal anesthesia is probably the most suitable for this condition. If it is considered better judgment to defer the laparotomy, general supportive measures should be employed to improve the general condition of the patient. An immediate para-

centesis abdominis should be performed in cases of marked distention to release any air contained in the abdominal cavity, thus relieving the pressure on the diaphragm. A physician administering emergency treatment should not hesitate to perform a paracentesis and release the air slowly. Many times following this procedure the condition of the patient will improve markedly and thus facilitate a subsequent laparotomy with a better prognosis.

The incision of choice is a left lower rectus or a low median line. The exploration of the abdomen should include as minute scrutiny as possible of the entire colon, the lower part of the ileum and the mesentery. The character of any fluid contained in the abdomen and the presence or absence of any gas with a fecal odor will suggest the severity of the injury.

If there is only a small amount of damage to the serosa and muscularis or a small perforation, these may be repaired very easily and quickly. Obviously, if there is great damage and repair is impossible, resection of the injured portions and the establishment of a colostomy are indicated. If the condition of the patient is extremely poor, it may save time and even the patient's life to bring the injured intestine into the incision as a colostomy (Andrews). More frequently, however, it would be wiser to complete the repair. When a resection is necessary and sufficient viable and movable intestine can be obtained, one should perform a lateral or end-to-end anastomosis. When an anastomosis is impossible, a colostomy should be established. One should not hesitate to establish an artificial anus above the injured area, especially when the damage has been extensive, in order to relieve the pressure over the affected portion, which has been repaired.

Whether to repair the injury and establish drainage higher up, perform a resection and do an anastomosis, establish an artificial anus or bring the injured portion into the wound as a colostomy is the responsibility of the surgeon and depends on the amount of damage to the intestine and the general condition of the patient.

The treatment indicated for injuries resulting from the oral introduction of air into the alimentary canal is determined by the judgment of the surgeon, depending on the degree of injury thought to be present and the condition of the patient. In general, it is palliative.

Postoperative Treatment.—This is largely a matter of symptomatic treatment, and it is necessary to deal separately with each condition as it arises. The patient preferably should be placed in the Fowler position. Distention, due principally to a paretic condition of the bowel, is to be expected, and may be relieved when feasible by the use of a rectal tube, milk and molasses enema, glycerin, turpentine and other enemas. Fluid depletion may be restored by the use of physiologic solution of sodium

chloride introduced by hypodermoclysis, by slow proctoclysis when possible and by the administration of physiologic solution of sodium chloride or dextrose solution intravenously.

CONCLUSIONS

1. Compressed air is used extensively in industrial arts, and it is important to educate the employees concerning its deadly, penetrative powers, especially since almost all of these injuries are caused by practical jokers.

2. Clinically, the sigmoid is the viscus most frequently ruptured.

3. Experimentally, the rectum supports the greatest pressure, and the sigmoid, ileum, esophagus, jejunum, transverse colon, cecum and stomach decrease in strength in the order in which they are mentioned.

4. The outer two coats of the colon generally rupture along the longitudinal bands; this is followed by marked herniation and subsequent perforation of the mucosa on the antimesenteric surface. In the remainder of cases the mucosa perforates on the mesenteric surface of the intestine.

5. In the small intestine, in somewhat more than 50 per cent of the cases, all of the layers perforated simultaneously on the antimesenteric surface, with slight laceration of the outer two coats and very little herniation of the mucosa. In the rest of the specimens, mesenteric ruptures occurred.

6. A higher pressure is required to rupture portions of the alimentary tract in children than in adults.

7. The average pressure required experimentally to perforate the various parts of the intestinal canal both within and without the abdomen is approximately 4.07 pounds per square inch.

8. Less pressure is required to rupture the intestine when the air is introduced more rapidly.

9. The general mortality is 56.81 per cent, the operative mortality, 44.82 per cent and the nonoperative mortality, 80 per cent.

10. Early release of intra-abdominal pressure and laparotomy for proper surgical disposition of the intestinal injuries offer practically the only hope for recovery of the patient.

Dr. George A. Bullwinkle made the accompanying sketches. Lieutenant Commander Fennimore S. Johnson, M.D., U.S.N., prepared the microscopic sections, Prof. H. W. Farwell, physicist, Columbia University, supplied the physical computations.

PRIMARY MYELOGENOUS SARCOMA COMPLICATING CYSTIC DISEASE OF THE HUMERUS

REPORT OF A CASE *

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Primary tumors of the bone characterized histologically by an unorganized growth of round cells, without appreciable intercellular substance, occupy an uncertain position among malignant neoplasms of the bone. In the literature one may find such varied designations of these tumors as "solitary myelomas," "undifferentiated osteogenic sarcomas," "round cell sarcomas of bone," "endotheliomas," "cellular medullary tumors," "embryonal tumors of bone marrow" and "myelosarcoma." Ewing's sarcoma, apparently a homogeneous clinical entity, has but recently [1] been segregated from this ill-defined category of tumors.

We have recently studied the available literature on primary tumors of the bone in connection with a confusing tumor of the humerus, removed from a patient of one of us (H. McK.), which clearly originated as a complication of preexisting cystic disease of the same locality. This tumor had microscopic characters in common with the group of myelomas, while a disseminated scanty fibrous, hyaline and osteoid intercellular substance and certain of its gross characteristics allied it to the osteogenic sarcomas. In view of these peculiarities, we believe that a description of this tumor and a discussion of its place among primary tumors of the bone will be of interest in the general study of sarcomas of bone.

Cystic disease of the bone is believed rarely or never to undergo malignant change into primary sarcoma of the bone. In the literature, we have found one such case reported by Helbing.[2] Beck,[3] in com-

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1. Ewing, J.: Endothelial Myeloma of Bone, Proc. New York Path. Soc. **24**:93, 1924. Kolodny, A.: Bone Sarcoma, Surg. Gynec. Obst. **44**:1-210, 1927, supp., part 2. Copeland, M. M., and Geschickter, C. F.: Ewing's Sarcoma: Small Round Cell Sarcoma of Bone, Arch. Surg. **20**:246 (Feb.) 1930; The Nature of Ewing's Tumor, ibid. **20**:421 (March) 1930.

2. Helbing, quoted by Beck.

3. Beck, C.: Ueber ächte Cysten der langen Röhrenknochen, Arch. f. klin. Chir. **70**:1099, 1903.

menting on Helbing's report, stated that if the roentgenograms are examined carefully, some sign of malignancy may always be found in cases in which the condition later becomes unquestionably malignant. The latter author cited a single case from his experience with "107 cases of osteosarcoma" which was confused with a cyst of the bone, but in which a slight break in the periosteum could be demonstrated. Bloodgood [4] stated that most central lesions of the bone are either giant cell tumors or osteitis fibrosa, said to be but phases of the same pathologic process, and that the central malignant tumors are almost exclusively metastatic tumors, myelomas or central chondromyxosarcomas. Recently, Geschickter and Copeland [5] advanced convincing proof that cysts of the bone, which usually are either giant cell tumors or osteitis fibrosa, are always benign. These authors stated that proved cases of metastasizing giant cell tumor are instances of osteogenic sarcoma of the chondroblastic series containing giant cell osteoclasts in response to cartilage formation. However, the two cases cited by Wanke [6] seem to be valid exceptions illustrating acquired malignancy in a previously benign giant cell tumor.

Instances of solitary primary malignant tumors of the bone composed exclusively of cellular elements resembling the round cells of normal bone marrow are rare. Kolodny [7] stated that only one case of solitary myeloma has been reported in the Registry of Bone Sarcoma of the American College of Surgeons. Solitary myelomas of the cranium are said to have been found by Morax [8] and Ewald [9] and by Riser and Sorel,[10] and of the ilium by Greengough, Simmons and Harmer [11] (case 11), but the conclusiveness of these observations is somewhat clouded by the lack of a complete autopsy in each case. Shaw [12] reported a solitary myeloma of the humerus following a frac-

4. Bloodgood, J. C.: How to Diagnose and Treat a Bone Lesion: I. Central Lesions, J. Bone & Joint Surg. **8**:471, 1926; Central Sarcoma of Bone, ibid. **9**:217, 1927.

5. Geschickter, C. F., and Copeland, M. M.: Recurrent and So-Called Metastatic Giant Cell Tumor, Arch. Surg. **20**:713 (May) 1930; Tumors of the Giant Cell Group: A Pathologic Entity, ibid. **21**:145 (July) 1930.

6. Wanke, R.: Ostitis fibrosa und Sarkom, Deutsche Ztschr. f. Chir. **201**: 358, 1927.

7. Kolodny (footnote 1, second reference).

8. Morax, M.: Myélome orbitoire et cranien, Presse méd. **18**:806, 1910.

9. Ewald: Wien. klin. Wchnschr. **10**:169, 1897.

10. Riser, and Sorel, R.: Plasmocytome intracranien avec paralyses unilatérales multiples, Ann. d. méd. **26**:385, 1929.

11. Greengough, R. B.; Simmons, C. C., and Harmer, T. W.: Bone Sarcoma: An Analysis of the Cases Admitted to the Massachusetts General and Collis P. Huntington Memorial Hospitals from 1911 to 1921, J. Orthop. Surg. **3**:602, 1921.

12. Shaw, A. F. B.: A Case of Plasma Cell Myeloma, J. Path. & Bact. **26**:125, 1923.

ture that had been treated by curettage and bone graft, in which complete recovery had been made. Rogers [13] and Geschickter and Copeland [14] each recorded a case of similar solitary myeloma of the femur. Another solitary myeloma of the humerus is to be found reported by Greengough, Simmons and Harmer [11] (case 20). Ewing [15] stated that he observed solitary myeloma of the tibia and femur, but he did not describe his cases. Multiple myeloma, while a rare disease, is encountered with greater frequency, and is more familiar. Accounts of this multiple skeletal disease with summaries of the literature and bibliographies are given by Versé,[16] Wallgren,[17] Geschickter and Copeland [14] and by many others.

Undifferentiated osteogenic sarcomas (Codman [18]), tumors that microscopically are "composed of round cells which show no tendency to form any known structure or tissue," are uncertain in their right to belong to this class of malignant tumors. As Codman further stated: "These tumors are round cell sarcomas occurring in bone and from their position are classed as bone sarcomas, not because they are known to have been derived from bone or bone elements." Tumors described as undifferentiated osteogenic sarcomas are to be found among the case reports of Buerger [19] (cases 3, 11 and 12), MacGuire and McWhorter [20] (cases 25, 26 and 27), Connor [21] (cases 10, 11, 45 and 49) and by Coley and Coley [22] (case 48). A few of these cases demonstrate definite affinities with the recognized types of osteogenic sarcoma by the presence of quantities of "spindle cells," while the remainder are similar to alleged solitary myelomas described by other authors. It is certain that these tumors do not comprise a homogeneous group.

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13. Rogers, H.: A Case of Solitary Plasma Celled Myeloma, Brit. J. Surg. **17**:518, 1930.

14. Geschickter, C. F., and Copeland, M. M.: Multiple Myeloma, Arch. Surg. **16**:807 (April) 1928.

15. Ewing, J.: A Review and Classification of Bone Sarcomas, Arch. Surg. **4**:485 (May) 1922.

16. Versé: Ueber Plasmozytome und myelomartige Wucherung des Knochenmarkes, Verhandl. d. deutsch. path. Gesellsch. **15**:62, 1912.

17. Wallgren, A.: Ueber die Natur der Myelomzellen, Virchows Arch. f. path. Anat. **232**:381, 1921.

18. Codman, E. A.: Bone Sarcoma, New York, Paul B. Hoeber, Inc., 1925.

19. Buerger, L.: Bone Sarcoma, Surg. Gynec. Obst. **9**:431, 1909.

20. MacGuire, C. J., and McWhorter, J. E.: Sarcoma of Bone: An Analysis of Fifty Cases, Arch. Surg. **9**:545 (Nov.) 1924.

21. Connor, C. L.: Endothelial Myeloma: Ewing, Arch. Surg. **12**:789 (April) 1926.

22. Coley, W. B., and Coley, B. I.: Primary Malignant Tumors of Long Bones, Arch. Surg. **14**:63 (Jan.) 1927.

REPORT OF CASE

History.—Miss E. S., aged 65, a patient of one of us (H. McK.), who for years had been employed only with her own housework, entered St. Joseph's Hospital on Oct. 1, 1929, for care of a refractured arm. In March, 1929, she had sustained a fracture in the distal one third of the left humerus as the result of a light fall over the edge of a rug at her residence. The patient stated that she definitely felt the arm "give way" before striking the floor. For about a year previous to this time she had experienced intermittent vague pains in the region of the left elbow. A roentgenogram (fig. 1*A*) taken at the time of this first fracture explained the occurrence of the break after such minor violence; there

Fig. 1.—*A*, roentgenogram of the left humerus taken on occasion of patient's first pathologic fracture; *B*, roentgenogram of the left humerus taken at the time of the second pathologic fracture. The arrow indicates the site of biopsy, a section of which is shown in figure 2.

was a circumscribed zone of rarefaction with long axis parallel to the shaft of the left humerus, which had left only a thin plate of cortex in the distal part of this bone. The appearance of this picture was consistent with that of a benign solitary fibrocystic lesion. In a roentgenogram of the pelvis and upper half of both femurs, taken at this time, no fibrocystic changes were seen in these bones. Following five weeks of immobilization, the patient regained full function of the arm, but intermittent pain, slightly more severe than previously, remained. About September 1, while drying dishes in her home, she suffered a spontaneous fracture at the same site, which was treated temporarily by immobilization in a sling, as this relieved the pain somewhat. Nothing further was done until the

patient entered the hospital. No other facts of possible significance were obtained from her past history, except that she had suffered for years from chronic "rheumatoid" pains on the right side from the hip to the knee.

Examination.—Physical examination revealed nothing inconsistent with her age except locally in the left arm, where edema of the arm and forearm and brownish pigmentation about the elbow were seen. Some crepitus was elicited in the distal third of the arm, and pain on pressure was evident over the same area. Examination of the blood on admission showed only a mild secondary anemia, with normal coagulation time. There were 4,320,000 erythrocytes and 5,350 leukocytes in the peripheral blood. Hemoglobin was 70 per cent. The differential enumeration of leukocytes showed polymorphonuclear neutrophilic leukocytes, 66; small lymphocytes, 20; large lymphocytes, 8, and "transitional cells," 6 per cent. The Wassermann and Kahn reactions were both negative. The blood pressure was 165 systolic and 90 diastolic. Only a trace of albumin was found in an otherwise normal urine. The temperature on admission was 98.6 F., but notable was the fact that from the second day following admission until discharge and after readmission on December 31 up to subsequent amputation of the arm, the patient had a persistently subnormal temperature, averaging from about 96.4 to 97 F., which rose from 1 to 1.5 degrees nearer normal after the amputation. After entrance into the hospital, the patient still complained of persistent pain. Roentgen examination (fig. 2) made just after entrance to the hospital demonstrated the same cystic lesion in this left arm as was discovered on the occasion of the patient's first fracture six and a half months previously, when she was attended by another physician. There was, in addition, an irregular transverse line of increased density, and on one side of the shaft of the humerus almost continuous with the previously mentioned line was a slight elevation of the periosteum. Elsewhere, the contour of the cystic lesion was even and regular. The possibility of a malignant tumor of the bone was entertained, and biopsy was done uneventfully under general anesthesia on October 17. The shaft of bone was sampled near the insertion of the triceps, posteriorly, at approximately the location indicated by the arrow in figure 1*B*. The curetted bone was described by a pathologist as a normal bone spicule, without inflammation or tumor. On reviewing these sections later, we discovered a few scattered foci of slightly pleomorphic cartilage cells (fig. 2). An operative diagnosis of cyst of the bone was made at this time. Between October 9 and November 8, the patient was given four deep roentgen radiations to the distal two thirds of the left humerus in the hope of preventing metastasis.

The patient stated that she obtained union and partial function of the left arm after leaving the hospital in November, even the pain being but trifling. About December 24, while dressing herself, she again suffered a spontaneous fracture with a subsequent amount of pain comparable to the previous spontaneous fracture. About three days later she was seized with a sudden agonizing pain in this arm, so severe as to cause her to cry out. These new intense pains continued intermittently until and after the patient's reentry to the hospital on December 31. The temperature and results of the blood examination and urinalysis were essentially insignificant on readmission and subsequently, with the exception of the persistent subnormal temperature, already described, and an abnormally large proportion of "transitional cells" among the blood leukocytes, on one occasion 6 and on another 18 per cent.

Roentgen examinations at this time revealed in the left arm (fig. 3) changes suggestive of malignancy and a fracture, probably pathologic. There were no

changes in the other bones, including the skull and pelvis, ribs and spine, except slight arthritic changes in the head of the right femur. A second biopsy was done through the old operative scar on the lower posterior aspect of the left arm, on Jan. 8, 1930. Immediately on completion of the incision through the thinned fibers of the triceps muscle, a soft grayish tumor mass was found on the outside of the bone. An operative diagnosis of sarcoma of the lower end of the humerus was made, and the wound was closed. Examination of a portion of the tumor tissue was made by a pathologist, who reported "a highly malignant bone tumor, probably a primary sarcoma." Dr. E. R. Le Count later concurred in the opinion on the malignancy of the tumor.

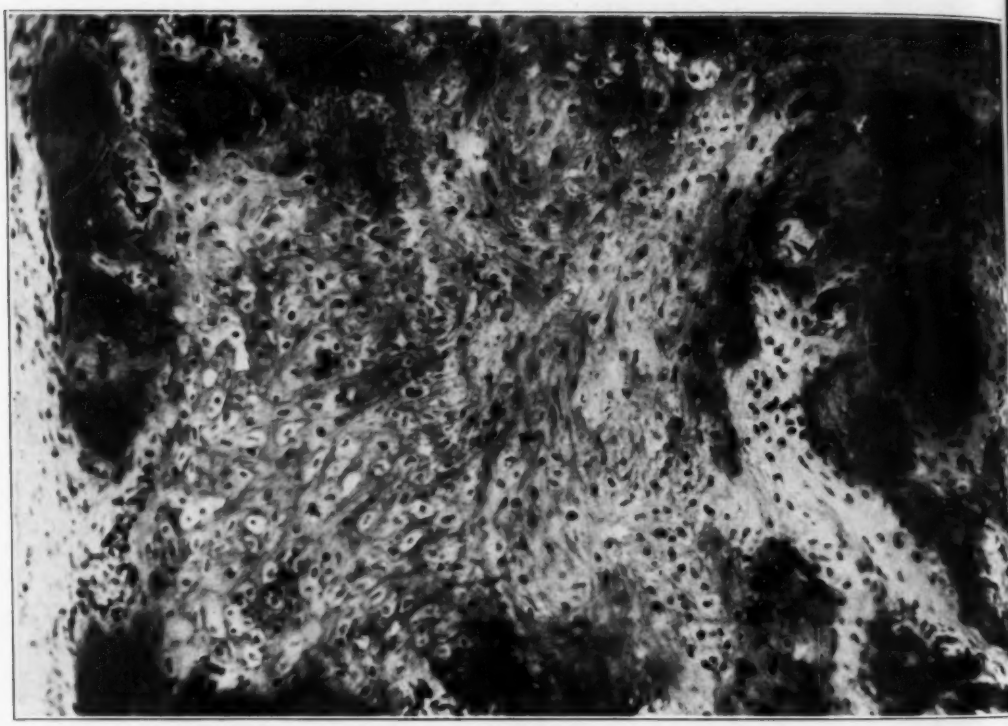

Fig. 2.—Photomicrograph taken of an area of pleomorphic cartilage cells found in biopsy sections done at about the time of the roentgenogram of figure 1 *B*. Reduced from a magnification of × 160.

Operation.—An amputation was approved by the patient, and was done on January 25, under general anesthesia. A preoperative roentgenogram of the thorax revealed a circumscribed nodule with a dense periphery in the upper left side of the chest near the apex, which was probably responsible for the observed displacement of the trachea to the right and for the slight fulness of the medial part of the left infraclavicular space. The patient stated that the latter had been present for years. The nature of this nodule was not definitely decided, except that it undoubtedly did not represent metastasis. Subsequent events proved this

to be true. The patient recovered without mishap from the amputation and was discharged from the hospital on February 8 in good condition. The patient has been in excellent general condition since the operation. At this time, twelve months following amputation, there is a local recurrence but no systemic metastases. Examination of the amputated specimen was begun three and one-half hours after completion of the amputation.

Macroscopic Examination.—The amputated left arm was still warm and soft. The soft parts were cut through about the middle of the arm, the humerus 8 cm. nearer the shoulder. The intact forearm and hand were attached. The skin of the upper part of the arm was smeared with blood. About the elbow, the skin

Fig. 3.—Roentgenogram of the left humerus taken at the time of patient's third pathologic fracture. Obvious signs of malignancy are present in this picture.

was stained with iodine in a zone from 5 to 8 cm. wide. The distance from the olecranon to the tip of the styloid process of the ulna, along the skin, was 26 cm.; that from the tip of the styloid process of the radius to the tip of the index finger was 16 cm. The width of the palm at the first distal transverse furrow was 77 mm. The maximum thickness of the hand was 22 mm. at the base of the hypothenar eminence. The skin of the palm was smooth, soft, pliable and wrinkled only by the usual creases. That of the dorsum was also smooth, soft and pliable, but was a faint yellowish brown, slightly wrinkled and abnormally motile over the underlying tissues. The skin of the forearm, not discolored by the yellow

referred to, was brownish yellow and finely mottled in places with a slightly darker color, and was smooth, soft, pliable and not wrinkled. There was an abundance of subcutaneous fat in the forearm. The width of the wrist at the level of the styloid process of the ulna was 57 mm. The width of the forearm at the elbow crease, with the arm in full supination and at as extreme extension as possible, was 105 mm. A full range of normal motion was possible at the wrist, and at all metacarpophalangeal and interphalangeal joints. At the elbow, extreme extension lacked from about 35 to 40 degrees of approaching a straight line, and forced flexion established an angle of only from 95 to 100 degrees between the arm and forearm. Supination could be completed, but forced pronation would bring the forearm to only about half the extent of normal complete pronation. The skin of the arm was smooth, soft and pliable, but was streaked with dried blood. There was even more subcutaneous fat in the arm than in the forearm, and the skin had about the normal amount of motion over the underlying parts. Externally, no abnormal structures could be felt beneath the skin of the forearm, hand, fingers or thumb. The maximum width of the arm was 125 mm. at 4 cm. proximal to the elbow. The circumference at the same level was 37 cm. A hard tumor was in the distal part of the arm, close to the elbow. This swelling had a limited amount of independent motion, and crepitated against the proximal parts of the humerus. The tumor projected externally, but slightly more on the internal aspect. The circumference of the arm at the edge of the skin made by amputation was 35 cm. Here the subcutaneous fat was abundant, golden yellow, and from 22 to 42 mm. thick. A small amount of divided muscle projected about 3 cm. beyond the skin, and still more proximal an almost denuded apparently normal humerus extended 5 cm. The severed nerves and blood vessels presented at the site of amputation. The exposed tissues were soft and pliable, and no abnormal structures or tissues had been bared by amputation.

When the skin of the arm and forearm was cut there was from 10 to 15 cc. of clear fluid in the subcutaneous tissues of the forearm. The abundant subcutaneous fat about the tumor was from 16 to 33 mm. thick; in the middle of the forearm, from 14 to 22 mm., and in the wrist, only from 1 to 6 mm. The weight of the skin of the arm and forearm, with this fat, was 1,250 Gm. The median nerve with the brachial artery and venae comites ran over the front of the tumor, the nerve being slightly flattened and compressed to about half of its diameter. The brachial artery ran between the median nerve and the tumor in a shallow groove, from 2 to 6 mm. deep, and gave off several fairly large branches into the anterior capsule of the tumor. The artery throughout its course was completely collapsed and contained nothing within its lumen. The venae comites contained a few drops of fluid blood. The ulnar nerve ran over the dorsomesial aspect of the tumor and descended abruptly, medial to the olecranon, being pushed ventrally from its normal position. The musculocutaneous nerve was entirely free from the tumor mass. Two grayish nodules, one 18 and the other 23 mm. in diameter projected into the subcutaneous fat, between the muscular septums, in the medial bicipital sulcus. Over a large part of the tumor mass the ulnar nerve was flattened to a varying extent, the maximum being about twice the normal diameter of the nerve. The radial nerve descended over the ventro-external surface of the tumor beneath the muscularis brachialis. This nerve was much flattened and compressed for 6 cm., largely on the front and distal surface aspect of the tumor, and then passed into the forearm. The muscles of the arm surrounded the tumor, except at the two places described, and were all firmly adherent on their undersurface to the capsule of the tumor. The muscularis

biceps brachii seemed to be little affected. The muscularis brachialis was markedly compressed and adherent to the outside of the tumor. The muscularis triceps brachii dorsally was somewhat atrophied. The common tendon of insertion of the long and medial heads of this muscle and the fibrous band between them filled a definite longitudinal furrow 50 by 10 by 5 mm. in the dorsal part of the tumor. Here the tumor seemed to have been prevented from encroaching on the extreme dorsal part of the arm. The color of all these muscles was the same as the muscles elsewhere, a deep reddish brown. The circumference of the tumor at the level of the previous measurements was 27 cm. It was incompletely surrounded by a tough fibrous capsule, distinct anatomically from the muscles, but adherent to many of them. In many places gray parts of the tumor projected through the capsule. Externally, the tumor seemed to be homogeneous with the consistency of soft cartilage, except dorsally, where there was a ridge of tough fibrous connective tissue from the humerus. None of the muscles originating on the humeral condyles and inserted in the forearm or hand had been invaded by the tumor. The synovial surface of the joint was smooth, glistening and yellowish gray, except for 22 by 12 mm. in the capsule just ventral to the trochlear articular surface of the humerus, where it was occupied by a grayish nodular tumor tissue. Three hemorrhagic areas, from 2 to 5 mm. in diameter, were within the grayish nodules replacing the synovia. The articular surfaces of the humerus, radius and ulna were all smooth, glistening, moist and of normal color.

The tumor was easily cut to a depth of 5 cm., when resistance was met. However, in places a small knife could readily be inserted entirely through the mass. The greater part of the growth lay ventral to the shaft of the humerus, which was markedly eroded and destroyed. On longitudinal section of the humerus and tumor (fig. 4), more of the anterior than of the posterior half of the shaft was found to be destroyed, as only small spicules of bone from 1 to 2 mm. in diameter remained over 6 cm. of the former site of the anterior half of the shaft. In the posterior half, there was a similar gap of only 3 cm. In this region, adjoining the remaining fragments of intact bone, there were also eight or ten small irregularly circumscribed zones of hemorrhage from 2 to 5 mm. in diameter.

The former marrow cavity was slightly bulged in the transverse diameter and free from bone over 8 cm. proximal from the trochlea. It was filled with grayish tumor tissue similar to that found in the extramedullary part of the growth. Beginning 8 cm. proximal from the trochlea and extending 31 mm. more proximal, the marrow cavity was filled with delicate, interlacing bony trabeculae, mixed with grayish tumor tissue. Over this same length there was a subperiosteal bony thickening at the junction of the tumor with the intact shaft and on both surfaces of the bone exposed by longitudinal section. The maximum transverse diameter of this thickening was 5 mm., thus making the total transverse diameter of the bone 28 mm. at a point 95 mm. proximal to the upper trochlear border. In contrast, 25 cm. more proximal, where the subperiosteal thickening was not present, the transverse diameter of the humerus was but 19 mm. This subperiosteal thickening was symmetrical on the two sides, white and of ivory appearance and consistency. At a point 105 mm. proximal to the upper trochlear surface, there was an irregular transition between the mixed intramedullary bony trabeculation and tumor tissue to apparently normal bone marrow, which extended proximally 110 mm. to the transverse surface of the bone made by amputation. The shaft of the bone over the latter extent was also apparently normal.

The extramedullary part of the tumor exposed by longitudinal section was completely surrounded by a white fibrous capsule of connective tissue, from the under surface of which from ten to twelve conspicuous and many more inconspicuous septums converged incompletely in the general direction of the center of the tumor mass, thus giving this mass the appearance of faint, irregular lobulation. These individual tumor units bulged slightly on this section. There was no gross bone or other differentiated tissue, save the previously mentioned radiating septums present on the background of the tumor in its extramedullary extent.

Fig. 4.—Longitudinal section of the gross specimen of amputated humerus with tumor. The larger part of the tumor is seen to be anterior to the shaft of the bone.

Microscopic Examination.—In sections of the curettement specimen removed from the arm in January and stained with hematoxylin and eosin, small irregular bits of tissue were composed largely of rounded or faintly polygonal cells, varying in diameter from 5 to 16 microns, the majority being from 9 to 12 microns. Two zones were seen within each of the irregular tissue units on the slide: a peripheral zone, composed largely of cells, the nuclei of which were solidly hyperchromatic with rare mitotic figures, and a central zone, composed almost exclusively of cells, slightly larger (averaging from 12 to 14 microns in diameter), the cyto-

plasm of which was frequently poorly fixed and thus ragged, but the nuclei of which were large and vesicular, with chromatin present in irregularly distributed hyperchromatic condensations (fig. 5). The latter cells tended to be in linear configuration, one or two cells in width. From one eighth to one sixteenth of these nuclei contained mitotic figures. In well fixed cells of either class, the nongranular cytoplasm varied in width on either side of the nucleus from 2 to 8 microns, averaging in the majority from 2 to 3 microns in width. Thus, the cytoplasm made up about one third of the cell. Delicate, sparsely nucleated

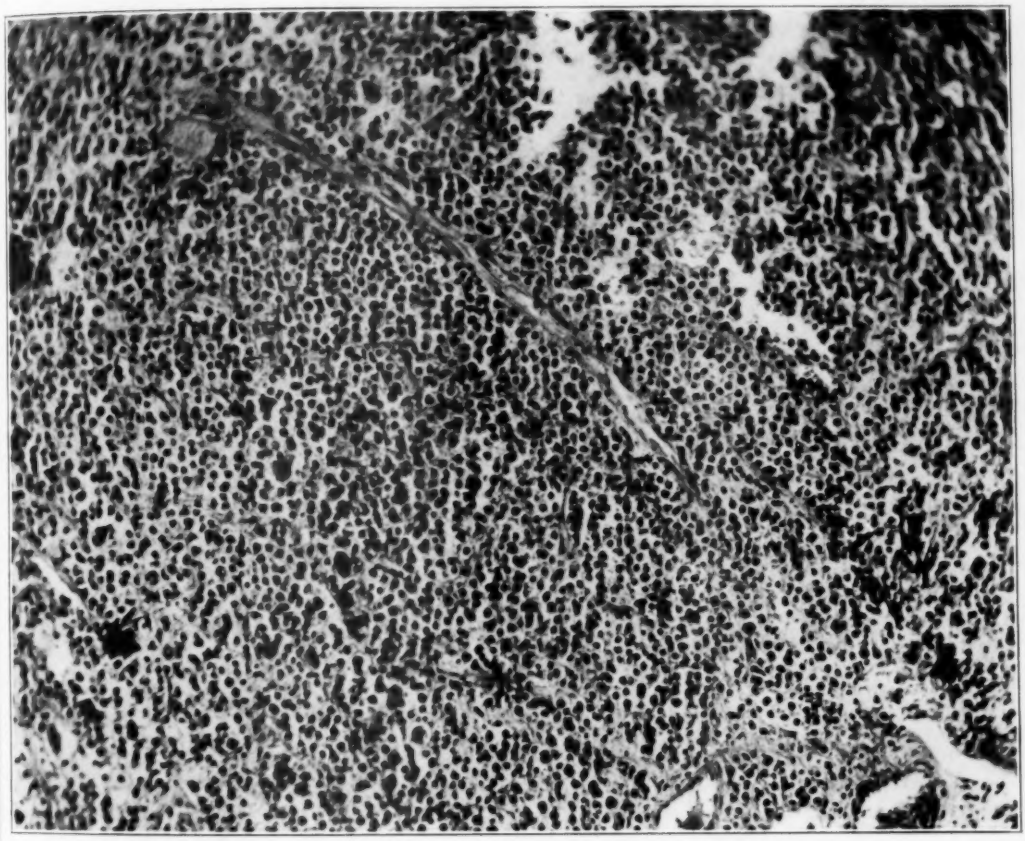

Fig. 5.—Photomicrograph of tissue removed at the second biopsy operation, done at about the same time as the roentgenogram in figure 3 was made; × 160.

stromal septums, from 8 to 30 microns in width, incompletely and irregularly divided the tissue into groups of from three to ten or twenty cells. Other wider, more cellular stromal units connected with smaller more regular fibrils. The nuclei of this heavier cellular stroma were sparse, but were composed about equally of small polygonal solid elements and of larger elongated paler elements, resembling but about twice the size of young fibroblasts. The last described stroma served as a matrix, carrying the majority of the small blood vessels. The distance between

successive larger fibrils varied from 250 to 1,000 microns or more, while that between the smaller acellular fibrillae was from 30 to 100 microns. In sections stained with phosphotungstic acid and hematoxylin, the larger stromal septums were a deep homogeneous blue, while of the smaller fibrils, about half were bluish and the other half a golden yellow. Although this stroma was described in detail, it was but an inconspicuous part, composing 5 per cent or less of the total tissue, which, as a whole, gave the impression of a cellular mass. Disseminated throughout the entire tissue, in no obvious relation to the smaller cells, were other much larger cells, varying in diameter from 16 to 22 microns, containing two or three nuclei, and in rare instances, even four or five nuclei, which overlapped one another and were symmetrically placed within the cell. In these cells the cytoplasm was abundant, varying from 5 to 11 microns in width, averaging 7 or 8 microns. The nuclei of these cells were rounded or oval, and were a deeply stained homogeneous mass. Mitotic figures were rare in them, being observed in only one in a hundred such cells picked at random. These larger cells were present in a proportion of from one to twenty, to from one to forty or fifty of the previously described smaller cells. They were so strikingly similar to these smaller cells that they had the appearance of being but hypernucleated variants of the same origin. At many of the edges of macroscopic tissue units on the slides there was a cellular condensation, varying in width from 5 to 150 microns, in which the cells were flattened with nuclei all solidly hyperchromatic, and from two to four times as long as they were wide. Disseminated throughout the tissue were numerous small capillary and thin-walled blood vessels, moderately distended with erythrocytes, varying in number, with different zones, from one to two, and from two to six or eight per high power field of a diameter of 380 microns. Many smaller irregular zones of hemorrhage limited and intersected by tumor cells were seen, as well as many small zones of hemorrhage about the periphery of the macroscopic tissue units of these slides.

In sections taken from five different locations along the periphery and extending from 15 to 23 mm. toward the center of the tumor, stained with hematoxylin and eosin, an identical picture was seen (fig. 6), save for the quantity and quality of stromal tissue present. The essential features of these sections were equivalent to the previously described tissue taken at biopsy. Like those sections, the tumor was seen to be composed largely of faintly polygonal, rounded and oval cells. Stroma was reduced to secondary prominence, although it was greater in abundance here than in the curettement specimen, since it was composed in this instance of from 5 to 20 per cent of the total area of these sections. In contrast to those sections, this tissue was more poorly vascularized. The occasional small blood vessels seen were devoid of erythrocytes.

Among cellular elements (fig. 7), the essential and prominent part of the tumor, four types of cells were seen intermingled at random, save the first cell type to be described, which was seen in greater abundance in close proximity to the larger fibrous stromal elements of the tumor. This cell resembled closely the small blood lymphocyte, having a single, round, heavily stained nucleus, but with relatively more nongranular cytoplasm than that cell. Mitosis was never seen in this small cell, the diameter of which, measured in twenty specimens, was almost constant at from 4 to 7 microns. Two other types, which together made up about 80 per cent of the cells, were practically identical, save that one possessed a single large prominent nucleolus, while its counterpart had no such discernible structure. These cells were large, variable in size, and were ovoid or polygonal, and mononucleated. They varied in size from 7 to 16 microns, many examples being found

of almost every dimension. Their cytoplasm was abundant and nongranular, making up from one fourth to one third of the total cell area. The nuclei were round or ovoid, varying in greatest diameter from 5 to 9 microns. Chromatin was present in hyperchromatic condensations, in the smaller cells of this class, making up three or four peripherally placed large blocks, and in the larger cells, six or eight smaller points, distributed somewhat more symmetrically within the nucleus. Mitosis was occasionally seen in these cells, but not with the frequency that it was observed in the same type of cell in the curettement specimen. Multi-

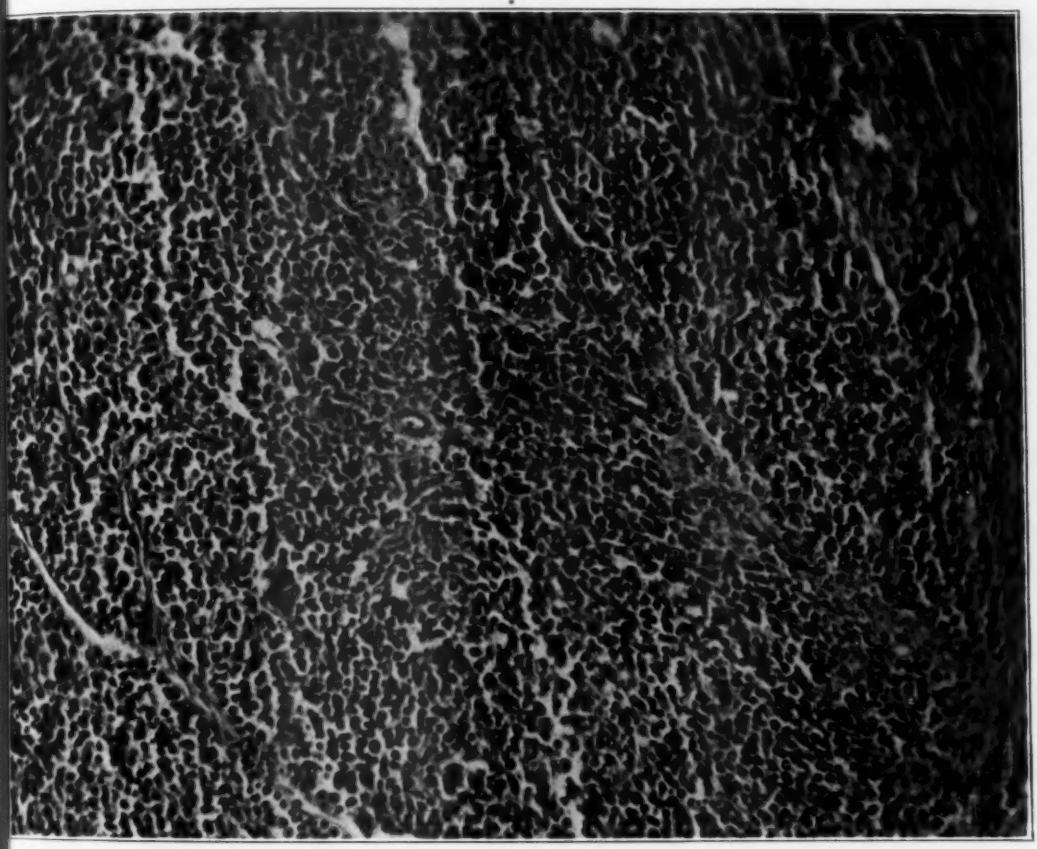

Fig. 6.—Photomicrograph of tissue from the periphery of the tumor taken from the gross specimen. The essentials of this picture are identical with figure 5; × 160.

nucleated cells were present in greater abundance than in the previously described curettement specimens, varying from the proportion in which they were found there to one in ten cells in certain areas in these sections. They varied in size from 14 to 22 microns, many being 16 microns in diameter. As a rule, they contained from three to five nuclei, but occasionally cells having from two to eight were seen. All of these nuclei were similar, being slightly ovoid, varying from 7 to 12 microns, with the majority 8 microns in greatest diameter, hyperchromatic,

and having multiple disseminated condensations of chromatin within the nucleus. Occasionally, mitosis could be seen in one of these extremely large cells, when they became especially hyperchromatic.

The stroma of the tumor in three of these sections was moderately prominent, making up from 10 to 20 per cent of the total area of the section. The relation of stroma and cellular zones of the tumor was not fixed, but varied markedly in different localities. Delicate white fibrous septums of connective tissue, with

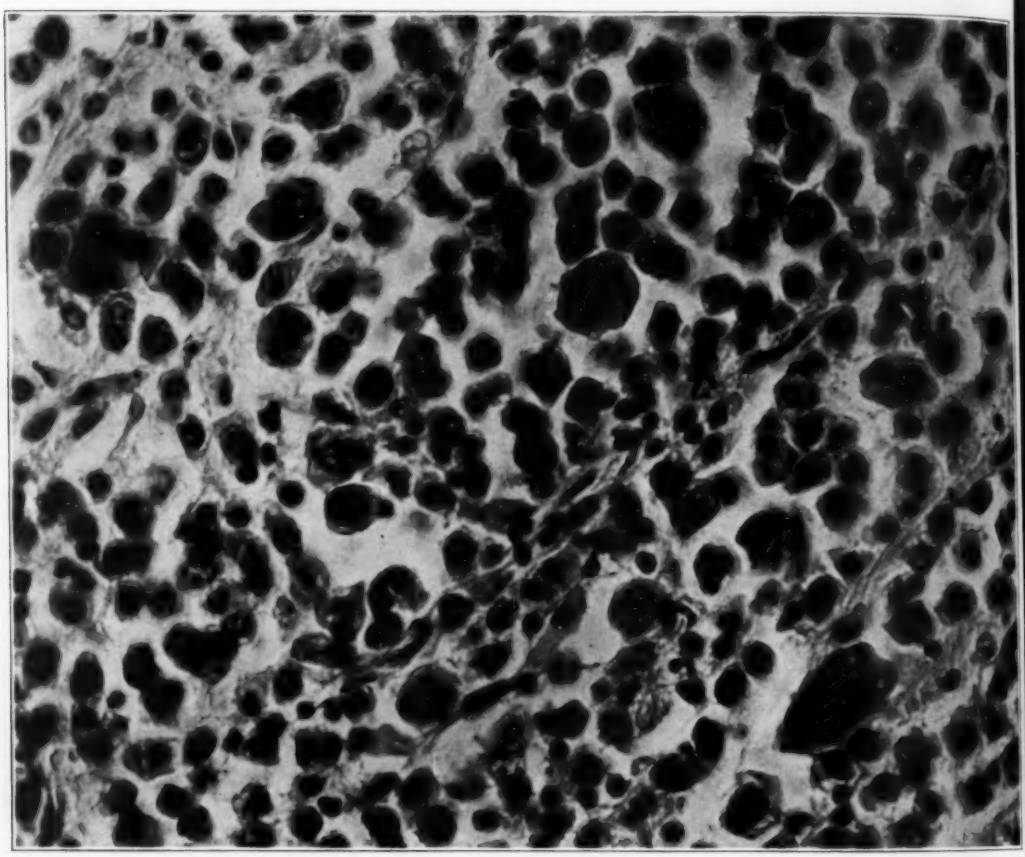

Fig. 7.—Photomicrograph showing types of cells to be found in this almost purely cellular tumor; × 630.

occasional fibroblasts present, irregularly and incompletely divided groups of from two to forty cells in width throughout the more cellular parts of the sections. Other wider stromal elements were present, of about half white fibrous connective tissue and the other half a more loose fibrillary structure, which, in sections stained with phosphotungstic acid and hematoxylin, gave the reaction of collagen. Fibroblasts and other irregularly heavily chromatinized cells, as well as cells that were definitely identical with the mononucleated cells of the cellular part of the tumor, were present in moderate abundance, trapped in the interstices

of this stroma. In some localities the transition between stroma and cellular areas of the tumor was sharp, while in others stromal processes became more delicate and intermingled with narrow columns of tumor cells. Irregularly shaped deposits of calcium were seen within about one fourth or one third of the zones of such stromal tissue (fig. 8). Tumor cells were never adjacent to the calcified areas, but definite noncalcified areas of the stroma were always interposed. In certain areas of stroma surrounded by fibrous connective tissue and in other localities set

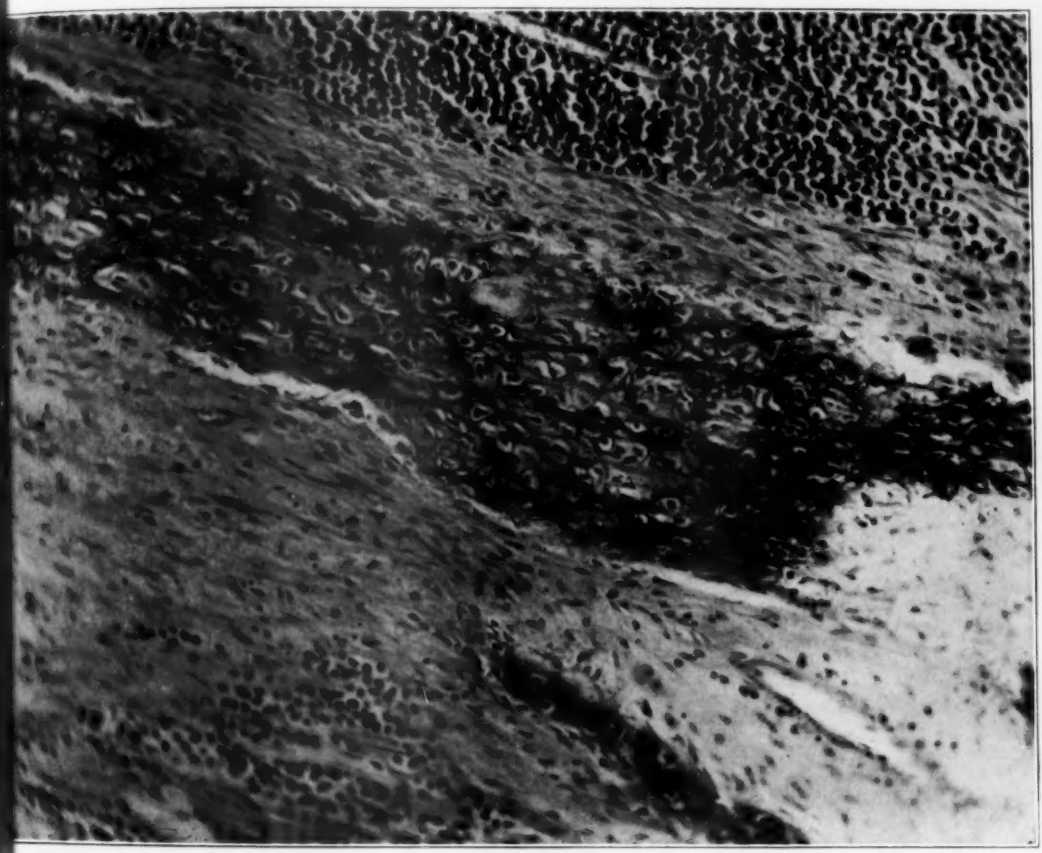

Fig. 8.—Photomicrograph showing partially calcified stroma to be found in the periphery of this tumor; × 160.

directly into an opening in the cellular part of the tumor, there were linear hyaline structures having a fixed width of about 20 microns, with fine, wavy, longitudinal fibrillae and with flattened marginal nuclei resembling in size and location the nuclei of striated skeletal muscle (fig. 9). All of the stromal elements described were not present simultaneously in two of the five sections, but various combinations of them were present in the other three slides. Thus this description is of the aggregate of stroma found in the peripheral 2 cm. of the tumor. Every gradation might be found in an extensive study of these slides, from a low power

field width composed almost exclusively of stroma to one exclusively cellular. A few blood vessels were to be found containing tumor cells in small numbers, admixed with erythrocytes. The capsule of the tumor was composed of a dense lamina of mature, white, fibrous connective tissue. Ten small, almost insignificant, spicules of lamellated bone were to be seen exclusively on one side of two sections. These represented the microscopic remnants of the destroyed shaft of the bone. These spicules differed from calcified stroma in that they were more

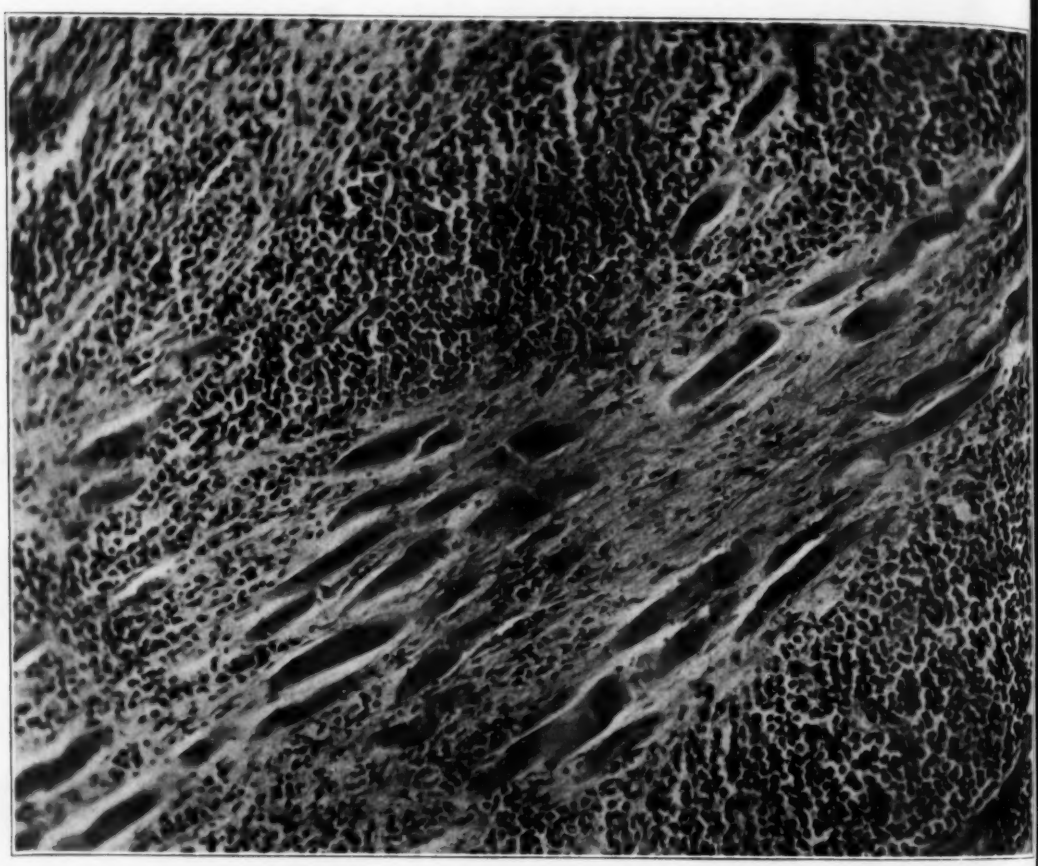

Fig. 9.—Photomicrograph showing hyaline substance, probably partially degenerated skeletal muscle, included in the periphery of the tumor; × 160.

deeply stained with the purple-blue of hematoxylin, were trabeculated and were surrounded immediately by tumor cells, some of which lay in definite small excavations, analogous to the lacunae of Howship. There were no large multinucleated osteoclasts. As a rule, the calcified stroma was not farther than 1 to 2 mm. distant from these bony remnants, all being from 25 to 30 mm. beneath the tumor capsule. In a single section, a definite wide band of stroma containing calcium deposits was seen 15 mm. subcapsularly and 10 mm. distant from the nearest spicule of lamellated bone.

COMMENT

According to the classification of the Sarcoma Registry of the American College of Surgeons, devised by Codman, Ewing and Bloodgood, malignant primary tumors of the bone include osteogenic sarcoma, multiple and solitary myeloma, angio-endothelioma and Ewing's sarcoma. A frequently found and confusing tumor is the benign giant cell tumor. Each type of this class of tumors has distinguishing characteristics.

The osteogenic sarcomas are osteoblastomas; that is, they arise from cells of the primitive mesoblast which are potential osteoblasts. Grossly, they originate in the metaphysis of the long bones, with frequently the clinical triad of trauma, tumor and pain. It is usually a disease of the young, the incidence peak falling in the second decade. However, no age group is free from the disease. Mirroring the age of the patient, and thus skeletal growth energy, are the gross anatomic types, the osteogenic and the osteolytic varieties of osteogenic sarcoma. Kolodny pointed out the fact, supported by the data of the Sarcoma Registry, that osteolytic tumors are more frequent in adults than in young persons. Grossly, and thus also roentgenologically, there are frequently seen beneath the raised periosteum calcified spicules arranged perpendicular to the long axis of the bone, in the characteristic "sun-ray" configuration. This is not an essential sign in osteogenic sarcoma, being conspicuously absent in the osteolytic varieties found more commonly in adults. Lipping of the periosteum by new bone formation at the junction of the tumor and intact shaft, the so-called "reactive triangle," is thought by Codman and other authorities to be an essential and cardinal sign of osteogenic sarcoma. The consistency of the tumor varies greatly, every gradation being seen, from the osteogenic types as seen in the sclerosing variety to the purely cellular osteolytic types. However, even in an extreme osteolytic osteogenic sarcoma there is said to be always a tendency toward bone formation, showing as a few scattered, sometimes microscopic, foci of new bone at some place in the tumor proper. The microscopic picture is varied, depending on the degree of differentiation of these descendants of the primitive osteoblast and the quality and quantity of intercellular substance. Kolodny dogmatically stated that "osteogenic sarcomata are never of the round cell type. If the leading cell of the tumor is a round cell, it is not an osteogenic sarcoma." Other authors (Codman, Ewing, and Simon [23]) are less insistent on this point.

Multiple myelomas comprise a characteristic clinical and pathologic group, occurring, in contrast to osteogenic sarcoma, largely in persons between the ages of 40 and 70 years, with the peak of incidence in the

23. Simon, W. V.: Die Knochensarcome, Ergebn. d. Chir. u. Orthop. **16**:364, 1923.

sixth decade. Multiple distribution of tumors, involving especially the short flat bones, as the ribs, sternum, clavicle, vertebrae and cranium, with slowly progressive anemia and cachexia punctuated by multiple and recurrent pathologic fractures, are the outstanding features of the disease. The roentgen rays show the tumor in the characteristic locations as rounded, punched-out areas or as a diffuse rarefaction of bone producing a mottled effect. Bence-Jones protein is present in the urine of many of these patients, but a similar proteosuria is associated with other tumors of the marrow cavity, notably metastatic carcinoma and endothelioma. Grossly, an outer table of parchment-like thinness is found in the affected bones, covering a dark red or gray gelatinous, freely bleeding tumor. The histology of multiple myeloma is typical. The tumors are composed of rounded or oval cells, usually with a single rounded nucleus and a scanty reticular stroma. Hypernucleated tumor giant cells with two to four nuclei are commonly seen. The cells in the majority of cases have been identified with plasma cells, although Geschickter and Copeland [14] stated that such cells do not take the characteristic plasma cell stain by the Unna-Pappenheim or polychrome methylene blue technics, and that such cells lack the perinuclear halo. In contrast, Versé,[16] relied on such positive signs in identifying his cases of multiple plasmocytomas. Although less frequent, certain multiple tumors are said (Kolodny, Ewing [24]) to be composed of cells resembling myeloblasts, lymphocytes and megaloblasts. Some formation of new bone and stroma occurs, as attested by the healing of pathologic fractures and by microscopic examination. Solitary myelomas, that is, tumors identical with the multiple tumors just described, but originating from a single focus, have not been found with frequency.

Angio-endothelioma, a rare tumor, is similar in its clinical aspects to osteogenic sarcoma. Its only distinction is a histologic one, cells being arranged in alveoli and tubules, traceable in some part of the tumor to proliferation of vascular endothelium. It is safe to say that such malignant tumors of the bone are correctly diagnosed only at autopsy, since in the reported cases, various diversified types of osteogenic sarcoma have been approximated clinically and roentgenologically. The possibility of metastatic carcinoma should always be deposed.

Ewing's sarcoma, although described by Ewing [25] himself as a diffuse osteolytic endothelial myeloma of the bone, has most recently been considered by Copeland and Geschickter [26] as a primary sarcoma of the bone originating either in the haversian systems or in some other

24. Ewing, J.: Neoplastic Disease, ed. 3, Philadelphia, W. B. Saunders Company, 1928.

25. Ewing (footnote 1, reference 1).

26. Copeland and Geschickter (footnote 1, third and fourth reference).

subperiosteal location. The group is considered as a highly homogeneous entity, characterized by recurrent attacks of pain occurring in a person practically always between the ages of 5 and 25 years, subsequently followed by tumor, which roentgenologically is seen to be a thickening of the shaft of the long bones in longitudinally concentric layers, later accompanied by widening and mottling of the marrow cavity due to internal bony destruction. The rarity of pathologic fracture, the exquisite sensitiveness of the tumors to roentgen therapy and the marked early tendency of the tumor to metastasize to other bones are further striking peculiarities of this tumor. Fever is commonly present in patients with Ewing's sarcoma in all stages. The soft parts of the tumors are firm and of a grayish white and divided into lobules by a number of radiating connective tissue strands. Microscopically, small, rather uniform polyhedral cells with scanty cytoplasm and rounded or oval nuclei make up the tumor. Multinucleated tumor cells are conspicuously absent. Fibrous trabeculation with hyaline-like intercellular substance divides the tumor tissue frequently to resemble an alveolar arrangement. So frequently are biopsy specimens diagnosed as inflammation of the bone that such a report alone should make one suspect this condition. Bence-Jones protein has never been found in the urine of these patients.

The benign giant cell tumor and allied conditions characterized by the presence of giant cell osteoclasts have recently been subjected to a thorough-going critical analysis by Geschickter and Copeland,[27] in which the relationship of these giant cell tumors as a progressing stage of the same type of lesion as osteitis fibrosa, a fact many times previously suspected, is reemphasized with new data. The tumor occurs largely in young adults, the peak incidence falling in the third decade, an age slightly beyond the average for osteogenic sarcoma and Ewing's tumor, although not an inconspicuous number of giant cell tumors occur in adults of all ages up to 50 or 55 years. The sites of bony involvement are the usual points of trauma to the skeleton: about the knees and shoulders and in the region of the trochanters and the distal part of the radius. The small bones of the extremities are occasionally involved, while in osteogenic sarcoma such a location is almost never seen. The tumor enlarges by central destruction with peripheral expansion and subperiosteal bony proliferation. The picture at any single moment depends on the relative preponderance of these two processes. Metastases are never observed in well scrutinized cases. Roentgenologically, an expanded marrow cavity is seen, usually with an intact thin bony shell about the periphery of the tumor. Internal bony trabeculation, almost

27. Geschickter, C. F., and Copeland, M. M.: Osteitis Fibrosa and Giant Cell Tumor, Arch. Surg. **19**:169 (Aug.) 1929; footnote 5.

universally present, is responsible for an appearance resembling soap bubbles. The solid portions of the giant cell tumors are friable and crumbly; thus pathologic fracture is common in this condition. The soft parts of the tumor within the cystic portions are soft, red and profusely bleeding when disturbed, thus having been likened to currant jelly. In the healing varieties, fibrous connective tissue and dense peripheral bone may predominate. The microscopic structure of the tumor has a single fixed characteristic: giant cells of the osteoclast type, which should be carefully contrasted with foreign body giant cells (Langhans) and tumor giant cells of other conditions. Numerous blood vessels are embedded in a stroma of elongated round or polygonal cells with large pale nuclei. Stromal cells are but slightly pleomorphic. In certain areas of many giant cell tumors can be found zones devoid of giant cells and poor in stroma and blood vessels, composed almost exclusively of rounded cells, zones that are similar histologically to myelomas, except that tumor giant cells are absent. The latter, however, are said to be absent in some varieties of myelomas. Clinically, with the slow but frequently progressive course, together with characteristic roentgenograms, the diagnosis of giant cell tumor is easily made in certain instances.

Atypical and borderline cases of malignant tumors of the bone are difficult to assign to one of the previously described categories. Frequently, the diagnosis can be made easier by the roentgenologist than by the pathologist. Particularly is this true of the cellular osteogenic sarcomas and of biopsy specimens taken by unfortunate chance from atypical zones of tumors elsewhere orthodox. In attempting to classify any tumor of the bone, data must be compiled from three sources: clinical, roentgenologic and pathologic, both gross and microscopic. The last item is a factor of marked variability among the osteogenic sarcomas. When, as in the present instance, a single of these aids is misleading, the clinical and gross pathologic data will furnish the most valuable clues to the origin and relations of the tumor. Roentgenography, as dependent on gross anatomy, frequently accurately supplants the latter in the living patient. From a consideration of the foregoing descriptions, the tumor in our case could have been either a cellular osteogenic sarcoma or a solitary myeloma. The sudden onset and development of the tumor in our patient, its location in the distal part of the humerus, the age of the patient and gross and microscopic pathologic changes all conclusively demonstrated that the tumor could not be a giant cell tumor. Likewise, it was highly improbable that our patient had Ewing's sarcoma, because of her age, the absolute dissimilarity in location of the tumor and its mode of growth and the gross and microscopic anatomy of the specimen.

The history of trauma, followed later by pain and tumor are characteristics that are shared by numerous tumors of the bone. Myeloma is usually a tumor with silent onset. However, the cases of solitary myeloma found in the literature prominently display trauma as a factor in the presumptive etiology of the condition. The relation of trauma to causation in this as in other tumors is not clear. The age of our patient (65 years) favored a diagnosis of myeloma, although it is not utterly inconsistent with osteogenic sarcoma. The subnormal temperature (averaging about 97 F.) during the time prior to amputation, with a rise of the temperature to a more normal range of 98 to 98.6 F. following amputation is suggestive of myeloma, being not infrequently observed in multiple instances of that condition. The occurrence of cells in the blood, designated as "transitional cells," in one instance to the extent of 6 per cent and in another to the extent of 18 per cent, is of interest. The lack of a definite description of these cells precludes the possibility of determining their relationship to the condition. Localization of the tumor in the distal third of the humerus is evidence against osteogenic sarcoma, according to certain authors. Kolodny stated that "an osteogenic sarcoma below the deltoid tubercle is a curiosity." However, the metaphyseal situation is suggestive of this condition. The gross appearance of the tumor was similar to the bone destructive variants of osteogenic sarcoma, definitely known to be more frequently seen in adults than in the young. Periosteal lipping at the junction of tumor with the intact shaft was present in this case. This single configuration is said to be pathognomonic of osteogenic sarcoma.

Microscopic analysis of the tumor leaves much to be desired as to the conclusiveness of an opinion, rendered from this source, as to the origin of the tumor. At first impression of a single section one was struck with the similarity to the microscopic picture of myeloma. However, the type could not be that of the most common of the myelomas, the plasma cell type, since, although a few cells having the typical appearance of plasma cells were seen with eccentric peripherally chromatinized nuclei, the majority of the nuclei were more pale, vesicular and placed symmetrically. Wallgren [17] and Christian [28] stated that the myeloma cell is a transitional form not to be classified as either a plasma cell or a myelocyte. The cellular zones of the tumor in our case, which, in the aggregate, composed from 90 to 95 per cent of the growth, had as a striking feature a moderate admixture of tumor giant cells, a characteristic frequently shared alike by osteogenic sarcomas and myelomas.

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28. Christian, H. A.: Multiple Myeloma: A Histological Comparison of Six Cases, J. Exper. Med. **9**:325, 1907.

The usual cellular osteogenic sarcoma is said to demonstrate a greater prominence of the spindle-shaped tumor cell rather than the retiring rôle that this type of cell played in this instance. On further search through more sections, a not inconspicuous fibrous and collagenous stroma was found, which in places was irregularly calcified, apparently arising as a product of cells morphologically similar to cells found in the purely cellular parts of the growth. This fact would tend to influence an assumption that the progenitors of osteoblasts had a rôle in the proliferation of this tumor. In sections of typical myeloma, no such intercellular substance is seen. These observations prove the thesis that a single biopsy specimen or a single microscopic sample of a malignant primary tumor of bone may be misleading. The microscopic analysis of a tumor of the bone is never complete until a composite of microscopic observations is synthesized into a single description.

The evidence (fig. 1 *A* and *B*) that a benign cystic lesion of the humerus was present prior to the onset of the tumor we believe to be definite. It is impossible to estimate accurately the actual duration of this condition, but, using symptoms of pain as an index, we believe that it must have been present for at least one year prior to the first fracture. In the roentgenogram (fig. 1 *B*), taken at the time of the second fracture, evidence is present in the slightly circumscribed elevation of the periosteum that is not inconsistent with the presence of a malignant tumor. Thus the results of biopsy at this time were probably misleading as by chance bone was taken that was not in contiguity with the suspicious raised periosteal zone. Microscopic preparations made from this material showed no definite alterations that would predict the condition soon to be obviously present. However, cartilage was seen in these sections (fig. 2). The relationship of this cartilage to the subsequent almost purely cellular tumor is not clear. We believe that the definite change in the patient's symptoms which followed a few days after the third pathologic fracture is significant. This was the symptomatic onset of sarcoma. The roentgenogram (fig. 3) taken during the following week showed unquestionably that a malignant tumor was present. The actual onset of this condition we would place a few weeks prior to the second pathologic fracture. If reasoning on this evidence is valid, sarcoma was present about three months before enough clinical and roentgenologic data were adduced to demonstrate this fact conclusively.

SUMMARY

On the positive evidence of bony periosteal lipping and the presence of a significant although small amount of stroma that could have been produced by potential osteoblasts, the diagnosis of an osteolytic myelogenous sarcoma is based. The age of the patient and the location in the

distal metaphysis of the humerus are rare qualities associated with this type of neoplasm. The majority of microscopic fields of sections of this tumor demonstrate a picture not inconsistent with myeloma, thus illustrating the deceptiveness of an incomplete histologic study of a malignant tumor of bone. We consider our case as an instance of a malignant neoplasm complicating cystic disease of the bone.

THE PRODUCTION OF HYPERPLASIA OF THE THYROID GLAND BY CHEMICAL MEANS

WITH SPECIAL REFERENCE TO PURINE BASES AND THEIR DERIVATIVES *

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In previous publications,[1] we have called attention to the hyperplasia, desquamation and loss of colloid that occur in the thyroid gland during the course of systemic infections and toxemias. This triad of changes in the thyroid gland seems clearly to be due to a demand for excessive function of the thyroid cells as a result of chemical or physiologic stimulation. It is secondary rather than primary, since the cellular changes obtained were brought about without any possibility of a direct local action of the bacteria on the thyroid cells. This explanation also adequately accounts for the loss of colloid and iodine in the gland. If it is assumed that the process is best explained on a chemical basis, one's attention is offhand directed toward the by-products of protein catabolism, since so many of them are known to be toxic, and because many of the bacterial toxins themselves are proteins.

Vaughan [2] held that the proteins of bacteria are best classified as nucleoproteins. He stated further that "all true proteins contain a poisonous group," and that this is liberated when the protein molecule is stripped. When faced with the fact that the splitting of proteins by enzymes or other chemical means may involve the liberation of vast

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* From the Department of Surgery, Washington University School of Medicine.

* Read at the Annual Meeting of the American Association for the Study of Goitre, Seattle, July, 1930.

1. Cole, W. H., and Womack, N. A.: Reaction of the Thyroid Gland to Infections in Oother Parts of the Body, J. A. M. A. **92**:453 (Feb. 9) 1929. Cole, W. H.; Womack, N. A., and Gray, S. H.: The Thyroid in Infections and Toxemias: Pathological Changes in the Human Gland, Am. J. Surg. **6**:221, 1929. Womack, N. A.; Cole, W. H., and Heideman, A. G.: The Thyroid Gland in Infections: The Effect Upon the Basal Metabolic Rate, Endocrinology **12**:773, 1928.

2. Vaughan, V. C.; Vaughan, V. C., Jr., and Walter, J.: Protein Split Products in Relation to Immunity and Disease, Philadelphia, Lea & Febiger, 1913, p. 18.

numbers of poisonous groups, we marvel at the manner in which the human body combats them and prevents their absorption. Some of these poisons need not be present in very large amounts to produce symptoms. A statement made by Kendall [3] seems significant in this respect, viz.: "The aromatic amines produced from the amino-acids—tyramine, phenylethylamine, beta-imidazolethylamine and indolethylamine—are physiologically active, even in very small amounts." We were also encouraged to investigate the by-products of protein catabolism, because the organisms that produced the most changes in the thyroid gland belonged to the group inhabiting the intestinal tract and possessing proteolytic and putrefactive qualities. It should be noted, also, that practically all the products of protein catabolism may be produced in the body by the enzymatic action of the secretions of the various organs on the proteins of bacteria or of the body tissues. For this reason, we have investigated the effect on the thyroid gland of the administration of some of the products of nucleoprotein catabolism. Of the constituents of nucleoproteins, the purine bases were chosen for experimental purposes because they seemed, perhaps, to offer the greatest possibility of toxicity to the thyroid gland Furthermore, the purine bases (adenine and guanine) are much more readily detached from the nucleoprotein molecule than the pyrimidine bases (cytosine and thymine). However, the exact derivative responsible for any toxic effect that might be produced by the purine bases would be difficult to determine, because, as Jones [4] remarked, "In the organism the purine groups of nucleic acid readily undergo deaminization with the final formation of the oxypurines, xanthine and hypoxanthine, and this is the case whether the nucleic acid originates from the food, from metabolism of the cell nucleus or from the bodies of dead leucocytes."

There can be no doubt that a close relationship exists between the thyroid secretion and the catabolism of proteins. Mathews [5] stated: "The great and predominant factor in the catabolism of protein is the internal secretion of the thyroid gland, thyroxin. This holds toward protein metabolism a position somewhat similar to that held by insulin in carbohydrate metabolism. Thyroxin hastens the oxidation of protein, and perhaps of other materials as well."

Histamine was the first chemical that we used in attempting to produce pathologic changes in the thyroid gland, since it is known to be formed in the body as a product of protein catabolism. Since the thy-

3. Kendall, A. I.: Bacteriology, Philadelphia, Lea & Febiger, 1928.

4. Jones, Walter: Nucleic Acids, New York, Longmans, Green & Company, 1914.

5. Mathews, A. P.: Physiological Chemistry, New York, William Wood & Company, 1925.

roid gland of the dog seems more susceptible to changes than that of other animals, we used dogs, for the most part, throughout. We found a definite desquamation with loss of colloid and beginning hyperplasia in the thyroid gland in two dogs in spite of the fact that the dosage given over the period of three days was insufficient to produce toxic symptoms of marked significance (fig. 1).

However, mindful of the possibility that the products of catabolism of nucleoproteins might be involved in the production of the changes in

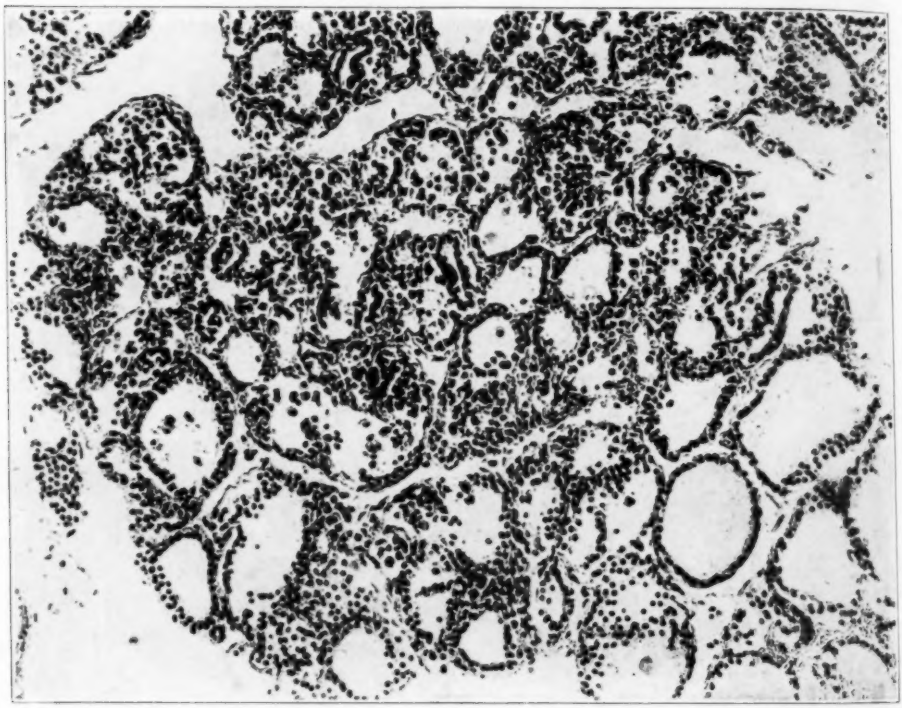

Fig. 1.—This section represents the thyroid gland of a dog which had received 133 mg. of histamine subcutaneously, divided into four daily doses. The animal exhibited signs of toxicity and was killed on the day following the last dose of histamine. The section was removed immediately after death. A loss of colloid, with desquamation of thyroid cells, and early hyperplasia can be made out. A small section of the thyroid gland was removed before administration of the histamine, and the gland was found to be normal in appearance.

the thyroid gland following systemic infections, we chose to investigate the purine bases and their derivatives. The purine bases themselves are expensive and difficult to obtain. With a small amount of xanthine (2-6 dioxypurine) available, an injection was made into one animal (dog). A definite desquamation of epithelial cells and loss of colloid

with beginning hyperplasia were found, even though the dose was insufficient to produce symptoms (fig. 2). On one occasion, we administered guanine, orally, but found no changes in the thyroid gland of the animal when it was examined post mortem a day or so later. The fact that the guanine was given by mouth and the xanthine intravenously may explain the impotency of the guanine. Although xanthine is not a direct component of the nucleic acids, both hypoxanthine and xanthine, as previously stated, are formed in the body during the catabolism

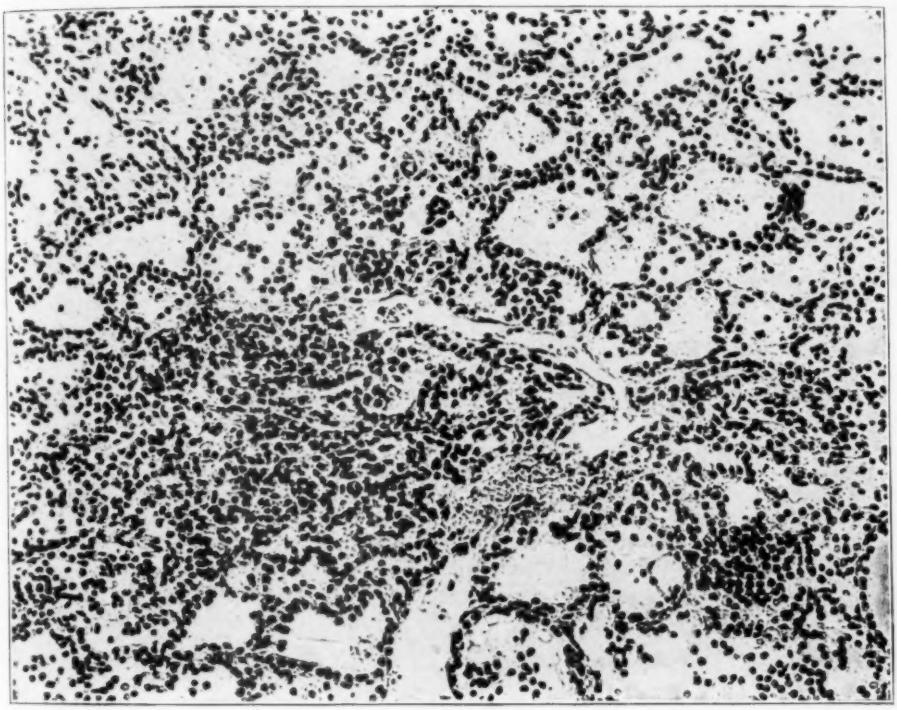

Fig. 2.—This section is from an animal that received 1 Gm. of xanthine (with the addition of a small amount of alkali to increase the solubility) intravenously in divided doses over a period of three days. No toxic symptoms were noted, but the animal was killed on the day after the last dose was given, and a section of the thyroid gland was removed immediately after death. Note the loss of colloid, the decrease in size of acini and the desquamation of acinous cells with early hyperplasia. It is significant that these changes were most pronounced at the periphery of the gland, whereas the central part revealed little change. A small piece of the thyroid gland was removed before administration of the xanthine, and the gland was found to be normal in appearance.

of nucleic acids by hydrolysis of adenine and guanine, respectively. Hypoxanthine is readily oxidized in the body to xanthine. By further oxidation in the presence of xanthinoxidase, an enzyme that is present in the human body only in the liver, the xanthine may be converted into

uric acid. To the present time, we have been unable to produce any changes in the thyroid glands of dogs by administration of uric acid even in such huge doses as from 1 to 3 Gm. per kilogram. Since xanthine and some of its methylated derivatives (see following paragraph), when administered to animals, do produce changes in the thyroid gland, it would appear that the intermediary products of the catabolism of proteins, especially the nucleoproteins, may be responsible for some or all of the deleterious effects observed.

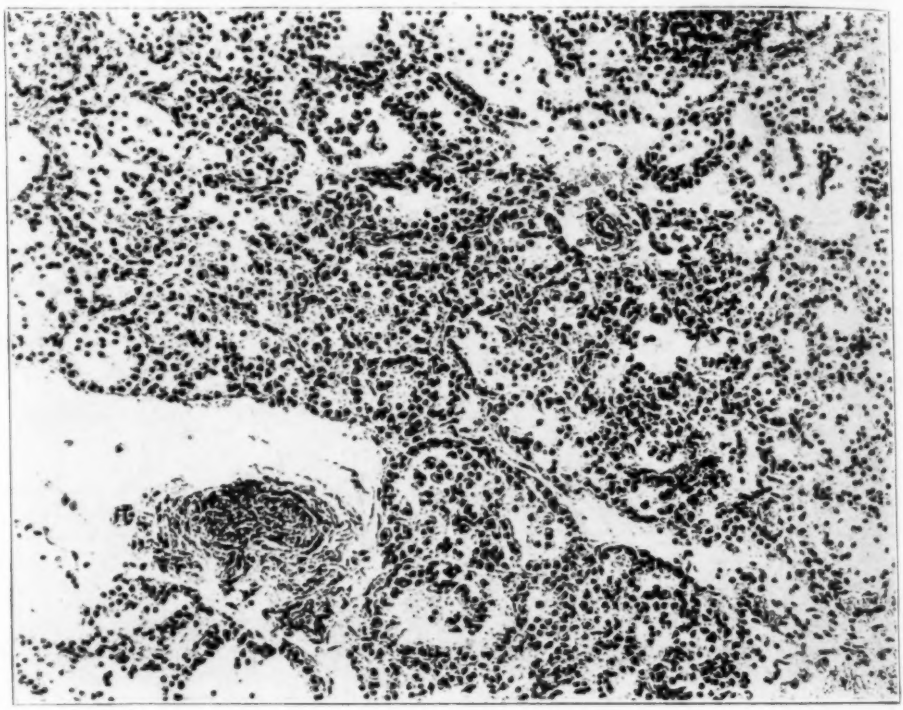

Fig. 3.—This section of thyroid gland was removed from an animal which died twenty-four hours after ingestion of 0.15 Gm. of caffeine per kilogram of body weight. A section removed a few days previously was normal in appearance. This illustrates how rapidly the colloid may be depleted and other changes, including desquamation and early hyperplasia, take place.

The methylated derivatives, caffeine (1-3-7 trimethyl-xanthine), theophylline (1-3 dimethyl-xanthine) and theobromine (3-7 dimethyl-xanthine), were used. When given to the point of toxicity, each produced desquamation, loss of colloid and beginning hyperplasia of the thyroid gland in dogs in practically every instance (figs. 3, 4, 5 and 7). Occasionally, the hyperplasia was so marked that the sections could

scarcely be differentiated from those seen in exophthalmic goiter of human beings.

In 1917, Means, Aub and DuBois [6] observed that when caffeine was administered to human beings in doses varying between 0.5 and 0.65 Gm., there was a constant rise in the basal metabolic rate varying between 7 and 23 per cent. The tendency for the methylated purines (including caffeine) to produce hyperplastic changes in the thyroid gland, as we have noted, may possibly explain this rise in the basal

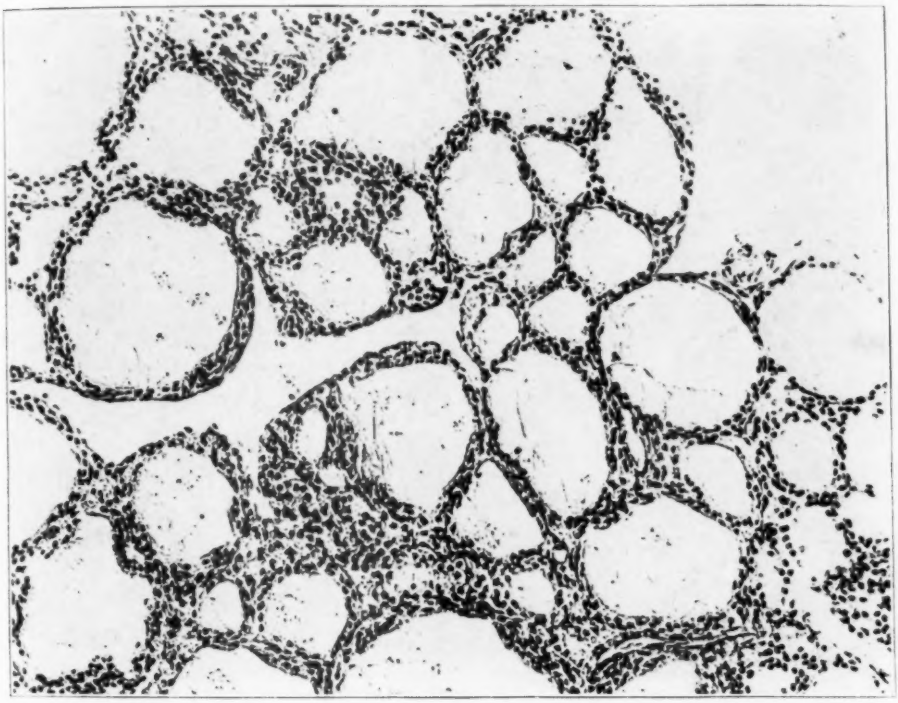

Fig. 4.—Section from a normal thyroid gland of a dog previous to experimentation. Note large acini (see fig. 5).

metabolic rate as a stimulative action of the caffeine on the thyroid gland and allied organs. Further support is lent to this theory by the remarks of Crile,[7] who has been a strong advocate of the theory that practically all the "stepping up" processes observed in the human being are expressions of hyperthyroidism.

6. Means, J. H.; Aub, J. C., and DuBois, E. F.: Clinical Colorimetry: The Effect of Caffeine on the Heat Production, Arch. Int. Med. **19**:832 (May) 1917.

7. Crile, G. W.: Thyroidectomy: Indications, Methods, Complications and End Results, Lecture delivered before the St. Louis Clinics, St. Louis, June 20, 1930.

Since the three methylated purine bases (caffeine, theophylline and theobromine) produce such striking changes in the thyroid gland,[8] when given to dogs in toxic doses, the possibility suggests itself that there may be other methylated compounds of similar nature in the organism, occurring in excess or abnormally during the destruction of protein. Although the better known of the methylpurines found in the human urine

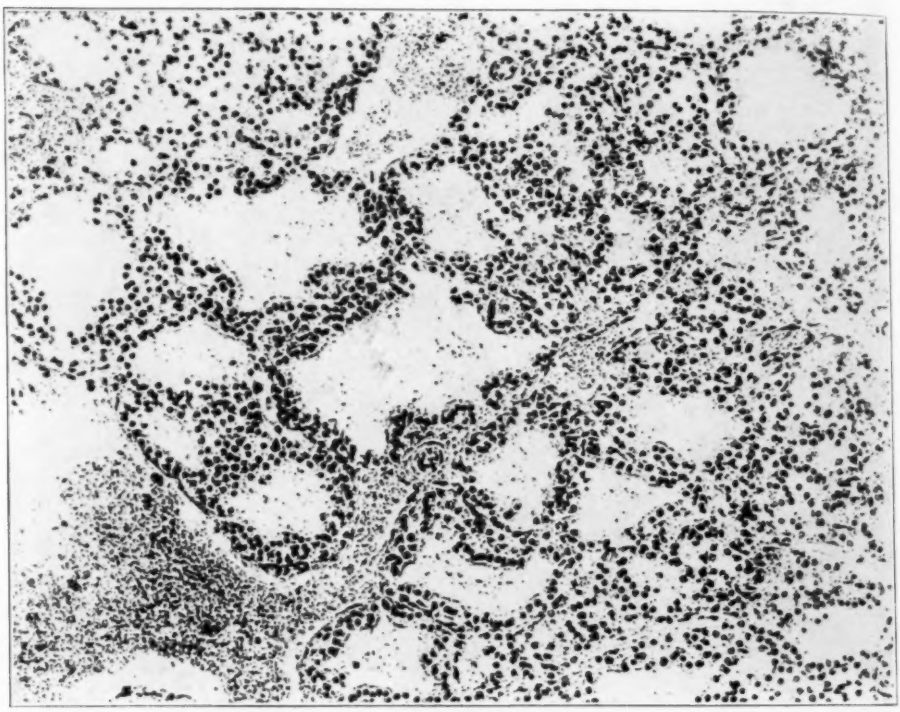

Fig. 5.—Section from the same thyroid gland as shown in figure 4, but removed from the dog following death caused by ingestion of 0.35 Gm. of theophylline per kilogram of body weight forty hours previously. Hyperplasia is the most prominent feature seen, although desquamation with decrease in size of the acini is present.

8. Even when confronted by the fact that the methylpurines will produce hyperplasia of the thyroid cells in dogs, we wish to emphasize that one cannot assume by analogy that the ingestion of methylated purine bases in beverages as consumed by human beings would have any influence on the production of hyperplasia in the thyroid gland. In the first place, if a relationship between methylpurines and hyperplasia of the thyroid gland exists in the human body, the offending chemicals would most likely be present as by-products of the destruction of protein. Moreover, the amount of methylpurines ingested in beverages would not be sufficient to exert any effect on the thyroid gland if the scale of dosage and effect in animals would apply to human beings.

(Kruger and Salomon [9]) probably have their derivation from ingested methylpurines, such as caffeine, etc., the fact still remains that the human body is able to methylate certain compounds and does so normally. In support of this statement such methylated compounds as creatine, creatinine, choline, epinephrine and neurine are found in the human body. Choline itself is present in the thyroid gland.

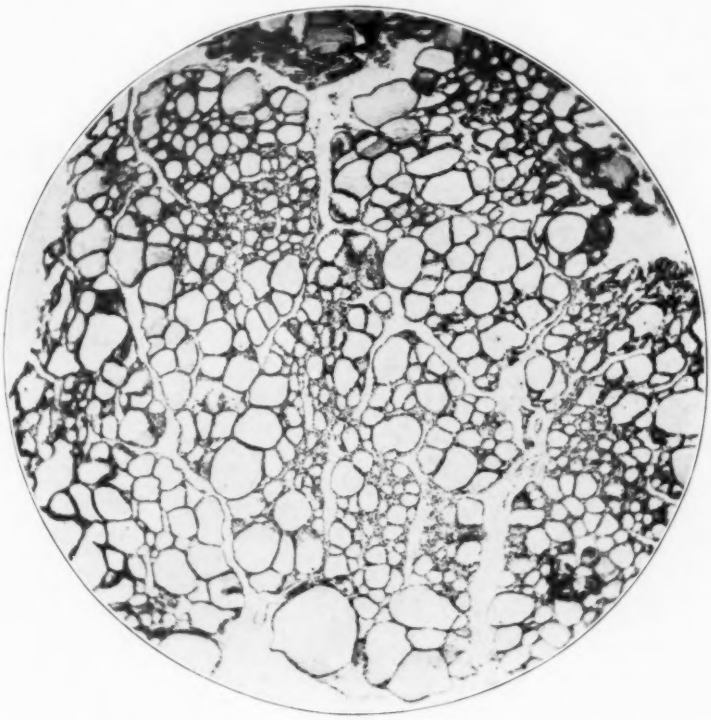

Fig. 6.—The appearance of the thyroid gland of a dog several days previous to experimentation. See figure 7.

A large number of chemical compounds (ninety) were studied with regard to their effect on the dog's thyroid gland. Of this group, caffeine, theophylline and theobromine were found to exert the greatest effect, especially of the hyperplastic type, on the animal's thyroid gland. A larger group (eleven), including xanthine, guanine, pyridine, quinidine, histamine, etc., were found to produce changes of a milder character. (Our attention was directed to quinine by Dr. Leon Bromberg.) The rest of the drugs used produced no effect on the thyroid gland, even

9. Kruger, M., and Salomon, G.: Die Alloxurbasen des Harns, Ztschr. f. physiol. Chem. **26**:350, 1898.

when given in lethal doses. It should be emphasized here that few drugs would produce marked changes unless given in toxic doses. We attempted to give all drugs in sublethal or lethal doses. It seems significant that practically none of a large series of inorganic drugs used produced any changes in the thyroid gland. For example, a dog weighing 10 Kg. was given 1 Gm. of copper sulphate orally per day for three days. The dog died on the day following the last dose. The liver

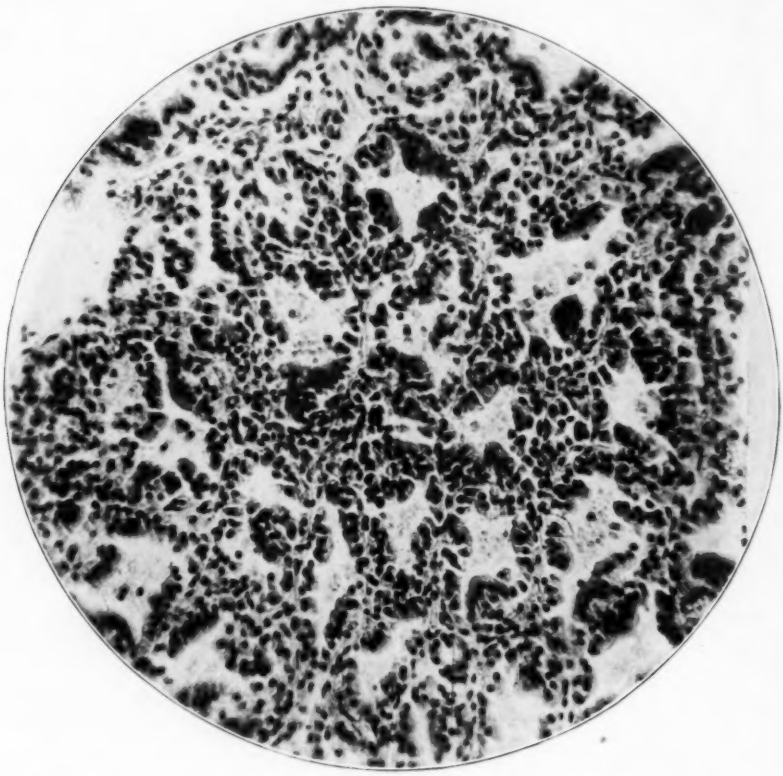

Fig. 7.—Section of the same thyroid gland as shown in figure 6, after the administration of 0.3 Gm. of theophylline per kilogram of body weight on one day, followed by a dose of 0.6 Gm. of theophylline the following day. This section was taken after death, which occurred about thirty-five hours after the first dose. Note the extreme grade of hyperplasia produced by the drug. However, such a severe grade of hyperplasia is produced only occasionally.

and kidneys revealed massive destruction of cells with hemorrhages everywhere, but the thyroid gland appeared normal.

On numerous occasions, sections were removed from the thyroid gland of a dog under ether anesthesia and another biopsy was performed from one to four days later to determine whether or not the anesthesia

and the operation produced any changes in the thyroid gland. No change was observed, except in one instance in which a loss of colloid with mild desquamation was noted in the thyroid gland of a dog in which a second biopsy followed the first by an interval of only one day. On the basis of this experiment, we now allow an interval of from three to four days to elapse after biopsy before experimentation. All animals with infected wounds following biopsy were discarded.

SUMMARY

In attempting to explain the effect (hyperplasia, desquamation, loss of colloid and iodine content) of certain infections and toxemias on the thyroid gland, which we and others have observed, we encountered certain noteworthy facts: The methylpurines—caffeine, theophylline and theobromine—on certain occasions produce a hyperplasia of the thyroid cells which is almost indistinguishable from the hyperplasia seen in the toxic goiters of human beings. We feel that since these drugs are so similar to the products of protein catabolism (especially those of nucleoproteins) the effect may be dependent on toxic by-products formed during the destruction of protein. It must be admitted and emphazised that the results obtained from the administration of most of the other drugs used in this series are subject to correction, since many of the drugs were used on only one or two occasions. We do feel, however, that the production of a marked degree of hyperplasia following the administration of certain drugs is significant, even though it does not occur in every instance. As a whole, inorganic drugs apparently do not produce many changes in the thyroid gland in animals, even after the administration of fatal doses. The results obtained in this report are preliminary. Further investigation is being done on the effects of drugs, especially of the by-products of destruction of protein, on the thyroid gland in animals.

THE FUNCTIONAL DISTURBANCES CAUSED BY THE INCONSTANT BONES AND SESAMOIDS OF THE FOOT*

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Much material has accumulated on the anatomic and roentgenologic aspects of the inconstant bones and sesamoids of the foot. The works of Pfitzner, Gruber, Bardeleben, and Dwight are classic. Much less, however, has been said on the ability of these bones to cause functional derangements of the foot.

We have been impressed, both from a study of the literature and from our experience in the foot clinic of the Hospital for Joint Diseases, with the frequency of these bones, and with the uncommonness of functional disturbances associated with these little bones. Many of these ossicles, from their unprotected position, are exposed to trauma. Most may be liable to any disease process that may affect any other bone; also, they may disturb the statics and dynamics of the foot. In our series—an analysis of 1,000 roentgenograms of the foot, with a study of 336 available histories of the 596 patients in the series—we have stressed the ability of these bones to produce functional disturbances of the foot. We have avoided any detailed anatomic, anthropologic and physiologic discussion, except so far as they affect our understanding of the situation.

The inconstant bones and sesamoids considered are: os trigonum; accessory scaphoid or os tibiale externum; os peroneum; styloid epiphysis and os vesalianum; os intermetatarseum; calcaneus secundarius (and calcaneonavicular fusion); os supranaviculare; secondary astragalus; os paracuneiforme; os subtibiale; bipartite internal cuneiform, bipartite cuboid, os proprium sustentaculi, cuboides secundarius, os unci; constant sesamoids of the great toe, and inconstant sesamoids of the other toes.

These ossicles are often called accessory bones. We think that the term inconstant bones is more appropriate, since almost every one of

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* From the Hospital for Joint Diseases, Service of Dr. Leo Mayer.

these bones has a separate cartilaginous center, preformed in the human embryo as early as the second or third month of fetal life, as proved by Bardeleben and others. Many of these ossicles are constant skeletal parts of the feet of lower mammalia. The majority of authors agree that these bones are to be considered as rudimentary elements inherited from the lower animals and present only in a more or less limited number of human feet.

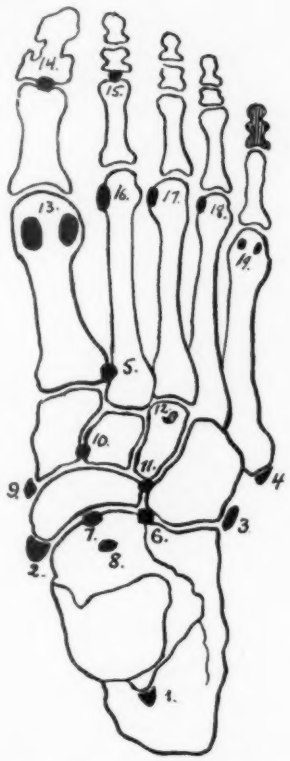

Fig. 1.—Diagrammatic ground plan of the inconstant bones and sesamoids of the foot: *1*, os trigonum; *2*, accessory scaphoid; *3*, os peroneum; *4*, styloid epiphysis and location of the disputed os vesalianum; *5*, os intermetatarseum; *6*, calcaneus secundarius; *7*, os supranaviculare (seen laterally best); *8*, secondary astragalus (seen best on lateral view); *9*, os paracuneiforme; *10*, os intercuneiforme (not described in text, since it can not be seen by roentgen examination and has no practical importance); *11*, cuboides secundarius; *12*, os unci; *13*, constant sesamoids of the great toe; *14*, interphalangeal sesamoid of the great toe; *15*, interphalangeal sesamoid of the second toe; *16*, *17*, *18* and *19*, inconstant sesamoids of the other toes. The shading of the terminal phalanges of the fifth toe represents the not uncommon fusion of the middle and terminal phalanx into one solid piece.

THE OS TRIGONUM

The normal posterior external tubercle of the astragalus is small. In our study, and in accordance with the concept of many authors (Gray, Dwight, Holland, and others), we have considered any enlargement or elongation of the posterior external tubercle due to fusion of the os trigonum with the small posterior external tubercle. Gray wrote: "This process (posterior external tubercle) is sometimes separated from the rest of the talus and is then known as the os trigonum." It is not

TABLE 1.—*General Statistics With Relative Frequency of Occurrence of the Different Inconstant Bones*

	Total Number
Patients	506
Histories examined	336
Roentgenograms of feet	1,000
Roentgenograms of feet showing an accessory bone or sesamoid anomaly	716
Negative feet	284
All age groups represented	

	Roentgenograms
Os trigonum noted in	493
Accessory scaphoid noted in	206
Os peroneum noted in	143
Styloid epiphysis of the fifth metatarsal noted in	43 of 24 patients
(There were 92 patients between 9 and 15 years of age, representing a total incidence of this epiphysis of 26.1 per cent)	

Calcaneus secundarius noted once
Os supranaviculare noted in 2 roentgenograms
Secondary astragalus noted in 2 roentgenograms
Os paracuneiforme noted in 1 case, bilaterally present
Os intermetatarseum noted 33 times

A combination of the os trigonum and the accessory scaphoid was noted 103 times; of the os trigonum and the os peroneum 35 times

A combination of the accessory scaphoid and the os peroneum was noted 23 times. A combination of the os trigonum, accessary scaphoid, and os peroneum was noted in 40 cases

unusual for this fused os trigonum to form a large, thick, blunt process, projecting posteriorly and possibly even abutting against the posterior rim of the tibia. Gallois and Japiot noted the posterior apophysis as from 10 to 14 mm. long in about 50 per cent of their cases; Mouchet and Bey noted a large posterior process in 38 per cent, Pfitzner in 14.3 per cent.

The secluded position of the os trigonum shelters it from trauma. It is for this reason that the bone has so little functional significance. Fracture of the free os trigonum is rare and seems to be almost impossible. The smaller the bone, the more difficult will it be to fracture it. Scherliess noted that in flatfoot the inwardly displaced astragalar head may render a fused or free os trigonum, projecting outwardly, more exposed to injury. A study of the literature reveals an old furore over the so-called Shepherd's fracture. Shepherd, himself, later realized that

his posterior fracture of the astragalus was only the free os trigonum. Experimentally, he was unable to duplicate this fracture. Cloquet and Hyrtl had made the same mistake many years before Shepherd. The work of Bardeleben and others established the os trigonum definitely as an inconstant bone. More recently, several observers, notably Patel and Bertrand, and Mouchet and Bey, have again brought up the possibility of Shepherd's fracture. After reading their articles, it is evident that they are impressed with the difficulty of diagnosing fracture from the os trigonum.

Menard has emphasized the fact that the appearance of the os trigonum, fused or free, is symmetrical. This is not necessarily true, and the general consensus denies Menard's views. It is not so uncommon to find the os trigonum free on one side and fused on the other. Bilateral fusion of the os trigonum is by far the most common observation. The consideration of symmetrical bilaterality, then, is not an

TABLE 2.—*Analysis of the Os Trigonum*

Os trigonum, fused or free, noted	493 times
Os trigonum noted free in	64 cases
Os trigonum bilaterally free in	14 cases
Os trigonum unilaterally free, other side not known, in	27 feet
Os trigonum free one side and fused on the other side in	9 cases
Os trigonum bilaterally fused in	102 cases
Os trigonum unilaterally fused, other side not known, in	115 feet

In a few cases, arthritic changes were seen in the os trigonum; otherwise, no changes of functional importance were observed

important point in the determination of fracture of the os trigonum. However, it is always best to have roentgenograms made of both feet for comparison. It should also be remembered that the os trigonum may rarely be bipartite or show a partial splitting. We have seen one such case. Pirazzoli, in a recent article, wrongly considered a partial splitting of the os trigonum as fracture. Some attention also has been given to the line of articulation between the os trigonum and the astragalus. It is usually smooth and clear, but occasional irregularities are observed, much as in the line of articulation between the accessory scaphoid and the scaphoid. Serration of the articular edge or fragment edges, with displacement of the fragment or fragments, may take place in fracture of the os trigonum. Pain about the posterior aspect of the ankle, on either inner or the outer side, may be due to many different lesions, and the coincidental presence of the free os trigonum need not be considered fact enough for the diagnosis of fracture. Bizarro noted a fracture of the os trigonum due to a rifle bullet.

On the other hand, it is much more possible to find fracture of a large posterior process, the detached fragment simulating a free os trigonum. A forced plantar flexion of the foot, with the large posterior

process impinging against the posterior border of the tibia, may fracture both the process and the posterior rim of the tibia. Forced dorsiflexion of the foot, with torsion of the posterior talofibular ligament (which inserts partially on the free or fused os trigonum) may detach a fragment. There may often be an associated fracture of the

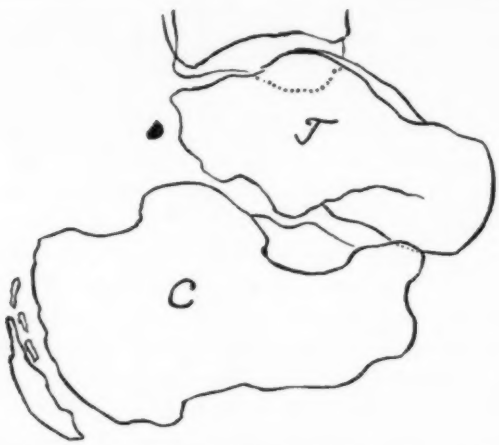

Fig. 2.—Beginning nucleus of ossification in the os trigonum, in the foot of a child, about 8 years old. In this and the following illustrations the abbreviations are as follows: *Ca*, os calcis; *T.*, os talus; *A.*, os astragalus; *S.*, os scaphoid; *F.*, fibula; *Cu.*, os cuboid; *C. I.*, os cuneiform I; *C. II.*, os cuneiform II; *C. III.*, os cuneiform III; *Ti.*, tibia.

os calcis or of the astragalus, with jamming of the process onto the os calcis. We recently saw a roentgenogram in which was shown a crush fracture of the os calcis, with jamming downward of the large

posterior process of the astragalus onto the os calcis. The process, however, was not fractured. Baastrup recently described several cases in which the posterior processes were enormous, long and large enough even to block normal plantar flexion. Eiken mentioned seventeen undoubted and six doubted fractures of the posterior process, in conjunction with fracture of the os calcis. In only one case was there an isolated fracture of the process. Lilienfeld noted that infraction of the posterior process is not so uncommon, both in his experience and in the literature. Dwight mentioned the fact that a loosely attached os trigonum might be pulled off by sprain of the attached ligament. It is doubtful whether the cases of Scherliess, Van Assen, Ebbinhaus and Vollbrecht are true fractures, the assumed fragment looking much like the os trigonum.

Clinically, it is noticed that the foot is held in the equinus and sometimes in the valgus position. There is definite tenderness about the ankle, usually posteriorly and medially. Flexion of the great toe may be painful, in view of the fact that the flexor hallucis longus lies in a groove, the outer border of which is formed by the posterior external tubercle. Weight-bearing is painful, and there may be an associated limp. Pain may be increased on dorsiflexion of the foot, and crepitation may be heard. There may be present associated fracture of the os calcis, the astragalus or the tibia. There is, of course, a definite history of trauma. The roentgenogram shows the detached fragment, no longer in the direct axis of the astragalus. The fragment edges may be serrated. Laquerrière stressed the fact that there must be an agreement between the clinical and roentgenologic signs. Treatment may be conservative or operative. A roentgenogram taken several weeks after the original accident should show the presence of callus, according to Nion.

Isolated disease of the os trigonum is rare. Ratto and Casanovas described a case in which, following a dog bite about the posterior aspect of the ankle, two fistulas developed, which discharged a serosanguineous pus. A probe passed through the external fistulous opening struck bone—the os trigonum—and the persistent presence of the fistulas was attributed to disease of this bone. The os trigonum was removed, with subsequent cure of the patient. The duration of symptoms had been two months. It is unfortunate that no microscopic study of the removed bone was made. It is our opinion that this was not an osteomyelitis of the os trigonum, but an inflammation of the soft tissues posterior to the ankle. The preoperative roentgenograms showed the bilateral presence of the os trigonum. Mouchet and Moutier noted an osteitis of the os trigonum in a boy aged 13½. No details of the case are given. We have never seen epiphysitis of the os trigonum. The os trigonum develops from a separate center of ossification, pre-

formed in cartilage at the second month of fetal life, which tends to ossify at about the eighth or ninth year. We have seen several roentgenograms of children's feet with small nubbins of ossification, representing the os trigonum. Arthritic changes in the os trigonum may be seen at times, usually in connection with a subastragaloid arthritis. Krida removed such a bone recently that was markedly enlarged by irregular osteophytes. Pfitzner found one os trigonum which was divided into several irregular pieces, a condition he thought pathologic.

Tumor of the os trigonum has never been reported.

THE ACCESSORY SCAPHOID

It is only the very large accessory scaphoid that usually gives rise to functional disturbance of the foot. The small accessory scaphoid or the accessory scaphoid with multiple centers of ossification is lost in the soft tissues posteromedially to the scaphoid and seldom causes trouble. The local effects of the large accessory scaphoid are due to the projection of this bone, medially or posteromedially. Fere and Denker, impressed by the marked prominence of this bone, called the condition exostosis. The shoe may press against this bony prominence, causing an area of redness, tenderness to pressure and sometimes swelling, the more so if the foot is turned in valgus. The skin may become thickened over the bone, and a protective bursa, which may be the site of an inflammatory reaction, may develop. No case of suppuration of this bursa has been described. Irritation of the tendon sheath of the tibialis posticus tendon is possible, according to Geist. Pfitzner has well described the variations of the tendon sheath, the tendon of the tibialis posticus, the bursa and the ligamentum calcaneonavicularis, which may exist in the presence of accessory scaphoids of varying size. Thus, tenderness may be present over the medial part of the tendon and over the medial fibers of the ligamentum calcaneonavicularis, both of which send fibers to the accessory scaphoid. Gaugele noted that a periostitis of the accessory scaphoid may develop from the constant small traumatizing of the bone. This tenderness must be distinguished from the not uncommon tenderness over the scaphoid in weak foot. One should also note the amount of motion of the accessory scaphoid over the scaphoid. Many authors (Bressot, Capette, Elmslie, Rendu and Pouzet, Santy, and others) have reported cases of such tarsalgia due to the presence of the accessory scaphoid. Cure is easily effected by conservative means, though many surgeons have removed the accessory bone.

Fracture of the tuberosity of the scaphoid is rare, and the detached fragment resembles the accessory scaphoid. The appearance of fracture

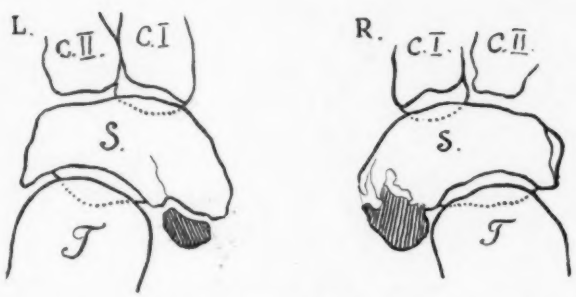

Fig. 3.—The accessory scaphoids are bilaterally present in the feet of a young woman about 30. Tenderness and pain were marked over the right accessory scaphoid following a sprain. The symptoms plus the roentgenographic appearance of the inconstant bone strongly suggested a fracture of the tuberosity of the scaphoid. However, a view of the foot taken in an oblique plane was more suggestive of accessory scaphoids. This case illustrates the difficulties that one may sometimes meet with in differential diagnosis with fracture.

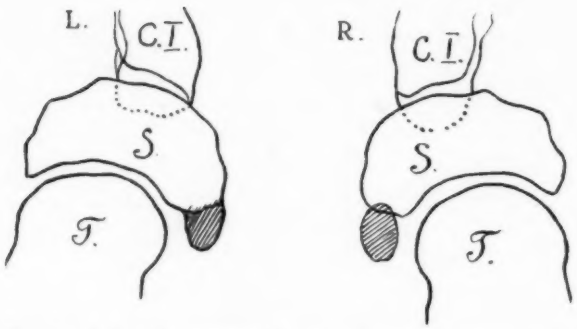

Fig. 4.—On the left side suggestion of beginning fusion of the accessory scaphoid to the scaphoid is seen. In this patient, a girl, aged 13, definite tenderness and pain were present over the left accessory scaphoid.

may be so striking that one may be tempted to diagnose the true accessory scaphoid as fracture, especially if there is a history of trauma. Many observers (Bazert, Horowitz, Haglund, Painter, and others) have made such an error. The Haglund-Lilienfeld controversy created a situation as interesting as the fight over the legitimacy of Shepherd's fracture. Haglund then maintained definitely that his cases were cases of fracture and not of accessory scaphoid. Case reports on actual fracture of the scaphoidal tuberosity are rare, Nicoletti, Lilienfeld, Mouchet and Landwehr having seen cases. In Landwehr's case, there was an associated fracture of the body of the scaphoid. Abadie and Rauge noted in their study of fractures of the scaphoid that the tuberosity may be detached. A differential point, aside from the serration of the fragment edge or associated fracture of other bones, is inversion of the base. The accessory scaphoid, when triangular, has its base externally and its apex internally; in fracture of the tuberosity, the base of the fragment is said to be internal. We have not seen this, however. It should be remembered that this fracture is uncommon, whereas the accessory scaphoid is frequently seen. The burden of proof is on the observer. Fracture of the tuberosity in the presence of a large accessory scaphoid has never been reported. Fairbank mentioned the case of a woman, aged 51, with a definite tarsalgia of about a year's duration. The accessory scaphoid was bilaterally present, but he thought the right one was fractured. Bipartite tarsal scaphoid (Froelich, Pirie), fracture of the body of the scaphoid and Kohler's disease of the tarsal scaphoid are easily differentiated.

Isolated disease of the accessory scaphoid has been reported. Arthritis of the line of articulation between the accessory scaphoid and the scaphoid is not unusual and is manifested roentgenographically by a haziness and irregularity of the joint surface. Clinically, there is definite tenderness over this joint with possible evidence of other arthritis in the foot. Dwight noted that there was a tendency of the cartilage of the joint to degenerate, with resulting interlocking of the apposing joint surfaces. Pain may be felt in the natural fusion of the accessory scaphoid to the scaphoid. This was noted by us in one case in a young adult. We have seen in a Negro, 55 years of age, detached, irregularly round, osteophytic particles from the scaphoidal tuberosity, which resembled the accessory scaphoid. The foot was strongly arthritic, and there was some resemblance to Charcot's disease.

In a previous note, we described the case of a girl, aged 8½, who had an unusual change in the accessory scaphoid and in the styloid epiphysis of the fifth metatarsal, which was interpreted as epiphysitis There was that fluffiness, that irregular patchiness of the bone, which suggested it strongly. There was complete restitution nine months later. Fairbank, several years before, mentioned that he had seen two such

cases. One of us (L.) has learned of two other cases at the Hospital for Ruptured and Crippled (service of Dr. Percy W. Roberts). In one case, the bone was removed, but unfortunately the specimen was lost. This condition should not be confused with a postulated and most probably theoretical epiphysitis of the posterior apophysis of the scaphoid, especially when it has a separate center of ossification, according to Froelich. Fairbank, in 1924, also described a condition of the accessory scaphoid similar to Kohler's disease of the tarsal scaphoid. There was noted fragmentation of the bone into two or more pieces, with condensation of the fragments. He terms this osteochondritis of the accessory scaphoid. Froelich, in 1913, also noted a similar condition. Japiot believed that an inflammation of the accessory scaphoid might give rise to a tarsalgia of adolescence. The pathologic process in the aforementioned diseases can only be inferred, since no specimens have been available for examination. Clinically, the conditions may be symptomless, or there may be pain and tenderness over the accessory bone. Froelich believed that there might be an osteitis of the accessory scaphoid due to infection with staphylococci of low virulence, as seen in one of his cases. Undoubtedly, the staphylococci in his specimen were due to secondary contamination. Froelich also believed that the presence of the accessory scaphoid rendered the midtarsal joints more open to infection. This has not been substantiated. Poncet's theory of fibrous tuberculous, and Kirmisson's theory of rheumatic, infection of the accessory scaphoid have not been upheld. Several authors (Bédart, Étienne) have mistaken redness and tenderness over an accessory scaphoid in tuberculous children as a tuberculous osteitis of the scaphoid, till a roentgenogram disclosed the presence of the accessory bone, to which all symptoms were due. Monahan's theory that the accessory scaphoid is present only in cases of constitutional disease is unwarranted.

Tumor of the accessory scaphoid has not been reported.

From the orthopedic standpoint, the major interest in the presence of the large accessory scaphoid is in its relation to flat feet. One may state that the accessory scaphoid may be present in a foot which is flat or not. The appearance of flatfoot may be suggested by the downward and inward projection of the inconstant bone. An analysis of such a foot will show that the forefoot and backfoot are in normal relation to each other. Gaugele noted that the presence of a weak foot is only incidental, and that the valgus position of the foot only exposes the inconstant bone to more trauma. In most of Geist's cases, a weak foot was not present; Hohmann noted the opposite. Zadek has pointed out that the major insertion of the tendon of the tibialis posticus is altered in the presence of the large accessory scaphoid, the insertion being mainly on the undersurface of the scaphoid. Together with this, it was

noted by Kidner that there is an inward, and possibly an upward, displacement of the tendon of the tibialis posticus. He then said that the alteration of the line of pull of the tendon and the alteration of its insertion tend to diminish the effect of the tibialis posticus as a supinator of the foot. The muscle in contracting must contract more strongly, since it is pulling at an angle, tending to weaken it and thereby diminishing its lifting power on the center of the arch of the foot. We do not believe that the slight inward deviation of the tendon of the tibialis posticus by even the largest of accessory scaphoids (from 1 to 2 cm. at the most) will result in a foot working at such a mechanical disadvantage that flatfoot will result. We believe that flatfoot is independent of the accessory scaphoid as a primary factor in its production, and that when the two exist together the relationship is incidental and not causal. Our experience substantiates this. It has also been noted that there is some limitation of hyperadduction of the foot with pain at the extreme of motion. This again may be due to secondary arthritic changes or static changes, the presence of the accessory scaphoid being incidental. In the hyperadducted position of the foot, there may be a crowding together of the soft tissues, between the large accessory scaphoid and the internal malleolus. Actual contact has not been observed. This, then, may be a factor in the production of pain.

Sitenko seeks deeper and invokes that constitutional condition causing the disturbance in ossification, which delays the ossification of the navicular bone, in the presence of the accessory scaphoid. The navicular bone, then, because of its delayed ossification, wedges itself in between the other, faster growing tarsal bones, thereby tending to flatten the arch. This statement is wrong, since the foot would go into adduction, as seen in congenital clubfoot, in which navicular ossification is delayed. Also, while it is true that in the scaphoid the nucleus of ossification appears later than in the other tarsal bones, it must be proved that the presence of the accessory scaphoid will further tend to delay navicular ossification. In the light of the definite anthropologic history of the accessory scaphoid, there is no reason why it should delay navicular ossification.

We believe that as a rule the accessory scaphoid should not be removed. There is no longer a tendency to remove the accessory scaphoid on sight. Undoubtedly, the small and medium-sized accessory scaphoids should be let alone; the larger ones, especially the long, hooked ones, may be removed only if there is enough functional disturbance to warrant it. In all of our cases conservative treatment, physical therapy, proper support for the shoe and exercises have given good results. All the operations used remove the accessory scaphoid and part of the tuberosity of the scaphoid. Several supplementary measures may

be employed—shortening of the tendon of the tibialis posticus, astragaloscaphoid arthrodesis and mobilization of the tendon after the method of Kidner.

Of the 336 histories examined by us, only 17 mentioned symptoms referable to the presence of the accessory scaphoid (206 accessory scaphoids represented). In no case was the accessory scaphoid removed, although in a young girl, a bilateral Miller operation was done by Dr. H. Finkelstein. In 4 there was definite pronation of the foot; in all, tenderness and pain over the accessory scaphoid were present; in 3, there was definite limitation of hyperadduction of the foot, while in only 1 were there bilateral symptoms. In 1 case, there was a gouged out area in the scaphoid bone, with tenderness and swelling, in the presence of the accessory scaphoid. It is questionable whether symptoms should be attributed to the accessory scaphoid. The Wassermann reaction was negative. Age groups represented here are: first decade, 1; second decade, 7; third decade, 3; fourth decade, 4. One patient was 43 and another 53. No attention was paid to sex in its relation to symptomatology in the presence of the accessory scaphoid.

THE OS PERONEUM

The os peroneum, wrongly called a sesamoid in the tendon of the peroneus longus, has seldom been considered as a factor in the production of tarsalgia. Stropeni, in 1920, reported a case of multipartite os peroneum, which he considered as a fracture. Histologic examination of the excised bone confirmed the diagnosis. His patient was an obese woman who fractured the bone in a momentary strong supination of the foot.

The bipartite character of the os peroneum has been noted often, more recently than in the purely anatomic era of Pfitzner and Gruber. No figures have been available as to how often the os peroneum is divided. We have noticed division of the bone in 34 cases (bone noticed 143 times in all); double division, 27 times; triple division, 6 times, and multipartite (4 or more pieces) once. There is, then, a definite tendency for the os peroneum to split. Lilienfeld and Pfitzner comment on this as an expression of greater regression of this inconstant bone.

We have introduced these preliminary remarks as fundamental for the understanding of a syndrome type seen by us in four cases. These patients complain of pain on the outer border of the foot, a variable distance behind the styloid process of the fifth metatarsal bone, usually definitely localized in the region of the os peroneum. The pain is often sharp; it may be definitely localized or may radiate up along the peroneal muscles. The patient may be confined to bed in the acute stage. Manipulation of the foot into varus increases the pain. There is no remembered history of trauma, although the patient may think that he

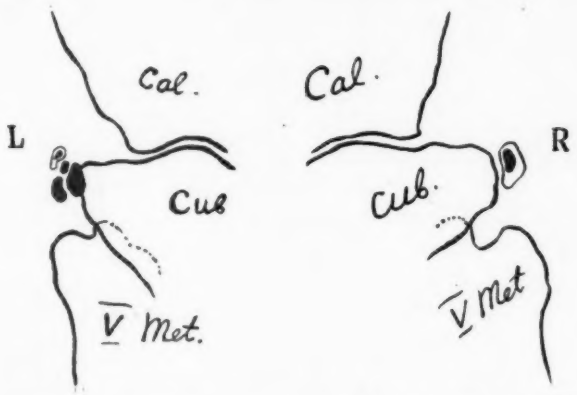

Fig. 5.—A multipartite os peroneum in the left foot. Marked pain and tenderness were present over the bone, suggesting the possibility of fracture. On right side os peroneum is bipartite.

has slipped or twisted the foot in some way. There is no history of recent infection. In two patients, both women, a history of an acute onset was given. We saw one case in the acute stage. The patient had a definitely suggestive tenovaginitis of the peroneus longus. The other patient's history also suggested an old acute tenovaginitis of the peroneus longus. Following this acute onset, there is a duller pain on the outer side of the foot, localized in the region of the os peroneum, the pain varying in intensity and appearing and disappearing. A roentgenogram shows that, corresponding to the region of greatest tenderness, there is a multipartite os peroneum, the bone being divided into four, five, six or more unequal fragments. There is no regular line of division between these pieces. In one instance, we were able to diagnose the presence of the multipartite os peroneum from a consideration of the symptoms and signs before the roentgenogram was taken. It is most difficult to fracture a small, slippery bone, partially enclosed in a tendon and protected by several layers of tissue thicknesses. Of course, the original presence of multiple centers of ossification may cause a predisposition to do so. The natural tendency of the os peroneum to regress must not be forgotten. Stropeni's theory of the production of fracture is that the os peroneum is crushed by a sudden inadvertent supination of the foot, the bone being fixed by a contracted peroneus longus. It is unfortunate that we have not been able to obtain any specimen for examination. The patients, after receiving strappings and physical therapy, improved somewhat. Most of them did not attend the clinic long enough to warrant any estimation of end-results. It may be noticed that we have hesitated to call this syndrome type fracture of the os peroneum. We have not enough data to warrant this. In two other cases, with histories and signs suggesting this syndrome, no os peroneum was seen in the roentgenogram.

It is unlikely that the os peroneum may be confused with fracture of the cuboid or os calcis.

Isolated disease of the os peroneum has not been described. Japiot believed that an inflammation of the os peroneum might well give rise to a tarsalgia of adolescence. Arthritis of the occasional articulation between the os peroneum and the cuboid has not been observed. This articulation, which is constant in the monkey, according to Gilette, is always rudimentary in man, according to Pfitzner. Schuster saw a case in which an unusually large os peroneum in a foot lacking in adipose tissue caused much pain on the outer border of the foot when a tight shoe was worn. Tumor of the os peroneum, as with the other inconstant bones, has not been reported.

In transplanting the peroneus longus the os peroneum may be encountered.

THE STYLOID EPIPHYSIS OF THE FIFTH METATARSAL AND THE OS VESALIANUM

Whether there is such a bone as the os vesalianum is still a moot question. It is apparent on examining the original drawings of Vesalius, that he himself precipitated the controversy. The dorsal and plantar views of the adult foot he presents are apparently of different feet. The dorsal view is a drawing of an undoubted os peroneum; the plantar view represents a small bone just behind the styloid process of the fifth metatarsal. This may be a forwardly placed os peroneum.

At any rate, the styloid epiphysis of the fifth metatarsal is not the os vesalianum. It is a definite accessory epiphysis (Gruber, Iselin, Kirchner) present in children between the ages of 9 and 16. Schouwey, continuing the work of Iselin, noted this epiphysis as constant between the ages of 13 and 14, fusion taking place at about the age of 16. Delayed appearance may occur in those who are ill. Gruber noted this epiphysis 18 times in 124 fifth metatarsal bones which showed an epiphyseal line. Lambert Rogers noted this epiphysis in 28.7 per cent; in our series it was present in 26.1 per cent of cases. Fusion is definite, and we saw no case in a person over 15 or 16 years of age.

Diseases of this epiphysis are rare. In some children, we have noticed redness and tenderness over the styloid process of the fifth metatarsal, in which the styloid epiphysis on roentgen examination was normal. It is possible that this condition may be due to a tight shoe pressing on a prominent styloid process. Iselin has described a definite epiphysitis of this epiphysis. Our reported case showed a lesion of the styloid epiphyses bilaterally together with a similar lesion of the accessory scaphoids. There were no symptoms. Roentgenologically, the styloid epiphyses were enlarged and showed fluffiness, irregular areas of density alternating with lighter areas. There was a definite tendency toward restitution, though this was not complete at the end of nine months.

The os vesalianum is a bony structure the existence of which it is necessary to prove with every case report. Any accessory bone must obey the postulates of Thilenius—that it is followed in the animal series, that it is present in the fetus and that it is connected by hyaline cartilage with its supporting bone. Little anthropologic work has been done on the os vesalianum. It is supposedly the atavistic remains of a fifth distal tarsal bone, such as that seen in the primitive reptile, *Sphen odon,* in *Proganosauria,* in *Didelphys* and in *Urodela.* It is also found in the tortoise. Spronck noted the os vesalianum formed in cartilage in a newborn child with polydactylia and other congenital deformities. This may possibly have been the distal tarsal element in the seventh ray, according to the ray theory of the development of the extremities (Debierre, Bardeleben, Albrecht, Bien). One of Laquerrière's cases

showed a large, well formed, bony element on the outer side of the foot, distinctly resembling a tarsal element. Despite the fact that he calls it the os vesalianum, this too may be considered as a vestige of the seventh ray. The cases of Baastrup, with the possible exception of one, show large bony elements, not in the least resembling the classic conception of the vesalianum. They are undoubtedly the large tuberosity of the fifth metatarsal bone partially detached, and probably may be a fracture of the tuberosity of the bone, since many of his cases have a history of trauma. Holland thinks that these are the separate tuberosity of the fifth metatarsal bone, developing from a separate center of ossification and persisting throughout adult life. It is noted that the condition may be bilateral. He includes these bony elements in his second class of vesalian bone, the first being the styloid epiphysis and the third the classic type of os vesalianum.

An analysis of each supposed case of os vesalianum reported is not within the scope of this paper. Suffice it to say that cases have been published by Gelinsky (one), Davis (one, and probably the styloid epiphysis), Hasselwander, Froelich (two), Mouchet and Moutier (five), Metzger (one), Fischer (two), Johansson (one), Laquerrière and Drevon (one), Holland (one), Mauclaire (one) and Gruber (three questionable ones). Haller, Diemerbroeck, Kulmus and Bartholinus mentioned the os vesalianum in the seventeenth and eighteenth centuries. Johansson noted that in his case the os peroneum was also present. To settle definitely the relation of this mooted bone to the styloid process and to the cuboid, roentgenograms in several planes—anteroposterior, lateral and several oblique—should be taken. Our impression from a study of the literature is that there is no bone that can be called os vesalianum. The so-called os vesalianum is either a forwardly placed os peroneum or a remainder of a seventh ray.

Any practical importance attaching to the os vesalianum, if it exists, lies not so much in its rarity as in distinguishing it from fracture of the tuberosity of the fifth metatarsal bone. Such fracture is not unusual, and the tendency is to call this fracture the os vesalianum rather than the converse. A history of trauma, the signs and symptoms present and a roentgenogram of both feet should help materially in making the diagnosis. It is safer to err on the side of fracture. It should also be remembered that the existence of the os vesalianum is still disputed and altogether denied by us.

The appearance of the os vesalianum may also be duplicated by a forwardly placed os peroneum.

OS INTERMETATARSEUM

The os intermetatarseum is said to be the base of the atavistic first ray according to Lunghetti, Dwight, Pfitzner and Volkov. Its location

between the bases of the first and second metatarsals may make it difficult to be seen. A dorsally placed os intermetatarseum may be seen on lateral view. It should not be mistaken for an arthritic exostosis or a calcification in a digital vessel.

Functionally, the os intermetatarseum is relatively unimportant. We have seen four cases in which it formed a dorsal and painful prominence, resembling an exostosis of the first cuneiform bone. In two of these cases, we were able to diagnose the presence of the bone before roentgenograms were taken. Young noted that the os intermetatarseum may be a factor in the production of a congenital hallux valgus. Schuster

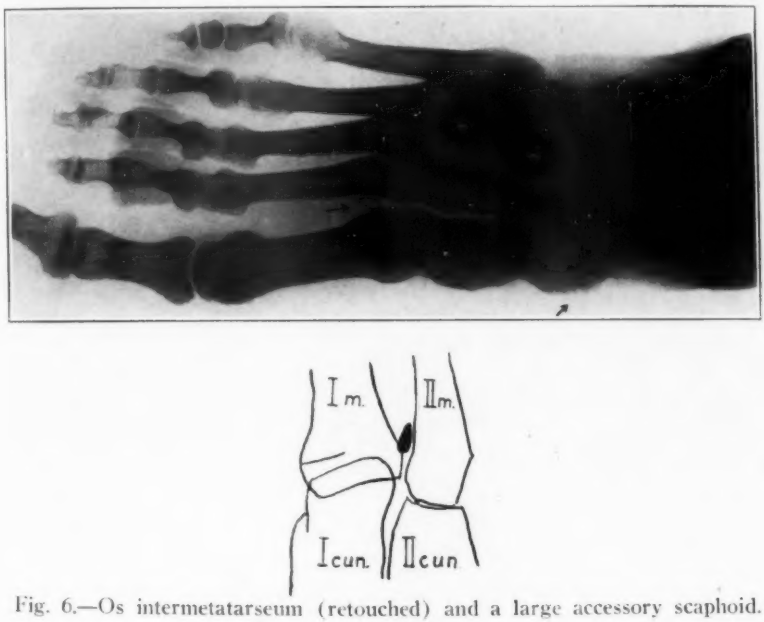

Fig. 6.—Os intermetatarseum (retouched) and a large accessory scaphoid.

said the same thing, and believed that it may cause increased adduction of the first metatarsal, with secondary abduction of the big toe. We have not noticed this.

This inconstant bone may possibly interfere in the operation of disarticulation of the tarsal-metatarsal joint.

CALCANEUS SECUNDARIUS AND CALCANEONAVICULAR FUSION

The calcaneus secundarius becomes important in disturbing the statics of the foot only when fused, either by fibrous or bony union, to both the navicular and the calcaneus—calcaneonavicular fusion. As a clinical and pathologic entity, this was brought forth by Slomann in 1921. Pfitzner, Stieda, Holl, Sutton, Hamant, Prouts, Dujarier,

Morestin, Zuckerkandl, Weber, Gruber and others had noticed the fusion in anatomic material. The manner of fusion, according to Pfitzner, occurred through the intermediation of the calcaneus secundarius, the quadrangular bone in the quadrangular space between the os calcis, scaphoid, cuboid and the astragalus. The calcaneus secundarius has been confused with two other bones, neither of which it is—the cuboides secundarius and a small bone, also called calcaneus secundarius by Dwight, at the front of the sustentaculum tali. We have not paid attention to the long anterior apophysis of the os calcis, which is con-

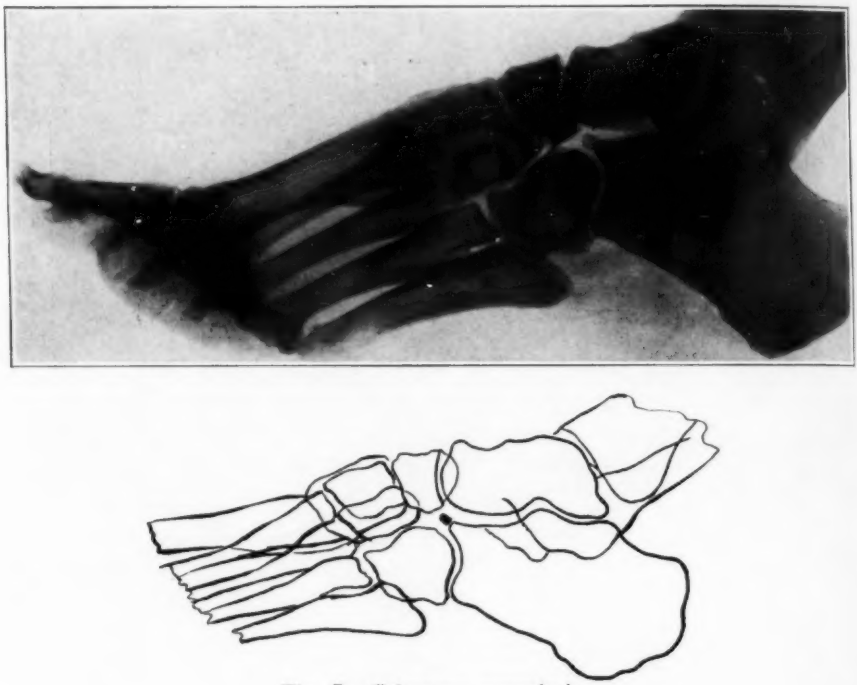

Fig. 7.—Calcaneus secundarius.

sidered by some to represent a fusion of the calcaneus secundarius to the os calcis. The two bones may be joined by amphiarthrosis, syndesmosis or synostosis.

Calcaneonavicular fusion is associated with important functional disturbances of the foot. Most cases show a definite and marked flatfoot, noticeable even in the young, but most noticeable at puberty. There is definite limitation of pronation and supination of the foot. The foot is often rigid, and the peroneal muscles may be spastic. Ankle motion is normal. There may be muscle atrophy, as pointed out by Chaput. The symptomatology varies with the degree and duration of the deformity. Symptoms are definitely increased during puberty. Not

many cases have been reported thus far. Slomann reported five cases, two in children and three in adults. He quoted Panner as having seen three undoubted cases. Nové-Josserand, in 1923, cited two cases, both of which Slomann denied. Badgley, in 1927, reported five cases; Bargellini, in 1928, one case, and Bentzon, in 1928, six cases. The fusion is uncommon, and misleading roentgenograms may tend to its diagnosis when it is not actually present. It is not unusual to see the anterior apophysis of the os calcis overlapping the scaphoid, simulating fusion, on the straight lateral view. An oblique view should show actual fusion best.

As with the accessory scaphoid, many theories have been set forth to explain the relation of calcaneonavicular fusion to the accompanying disability of the foot. We believe a simple mechanical explanation best. Lazarus believed the condition to be due to fetal persistence. In the new-born child he noted adduction of the foot, with the cartilage of the os calcis in contact with the cartilage of the scaphoid. Separation occurred in the normal detwisting of the foot, the interosseous ligament forming in the newly formed space between the navicular and the os calcis. The synostosis is only a persistence of this early condition, with imperfect development of the ligament. Leboucq also noted this. Bargellini believes in no one special theory in view of the fact that there are multiple anomalies of the os calcis, scaphoid and astragalus. The multiple action of all these anomalies, plus static factors, will produce a tarsalgia, usually at the period of greatest skeletal growth. Slomann's conception, previously enunciated in 1890 by Leboucq, we believe correct, namely, that the anterior component of body weight is transmitted through the body, neck and head of the astragalus, downward and forward to the navicular. Normally, this anterior component would pass through the navicular to the first cuneiform and first metatarsal bone. Owing to the fusion, there is a sudden stopping of the anterior weight forces at the navicular bone, with direct transmission vertically to the foremost and innermost point on the os calcis. This tends definitely to pronate the os calcis, astragalus and scaphoid. Nové-Josserand stated that flatfoot is secondary to the tarsalgia, which is due to a spasm of the extensor and peroneal muscles and to the diversion of articular movements to nearby joints because of the synostosis.

Because of the unusual pressure of forces at the talonavicular joint, osteo-arthritic changes may develop and complicate an already complicated disability. Treatment varies with the case, from the conservatism of physical therapy, exercises, manipulations and plates, to the more radical open operation—lengthening or excision of the peroneal tendons to relax spasm (Badgley), resection of the synostosis with or without interposition of the muscle belly of the extensor brevis digitorum to create pseudo-arthrosis (Badgley, Bentzon), wedge resection of the

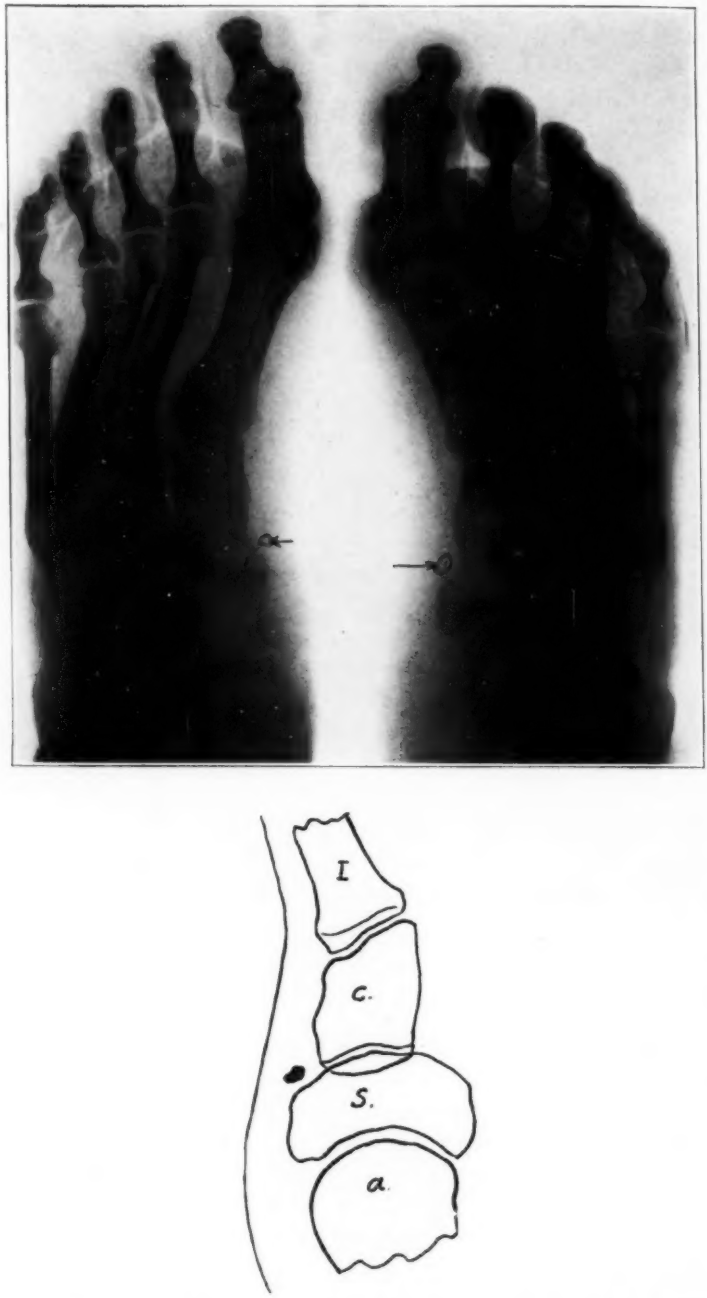

Fig. 8.—Os paracuneiforme (retouched). This is fairly well shown on the original plate, although it has photographed indistinctly because of poor calcification of this bone, which evidently is undergoing degeneration.

scaphoid to raise the longitudinal arch (Bargellini) and triple arthrodesis if the secondary arthritis is marked (Badgley). Krida removed a secondary os calcis with definite relief from pain, for which the inconstant bone was blamed.

In our series, we saw no case of calcaneonavicular fusion. We had only one case of unilateral calcaneus secundarius. (Although there was a history of a trauma, we believe this case to be a real inconstant

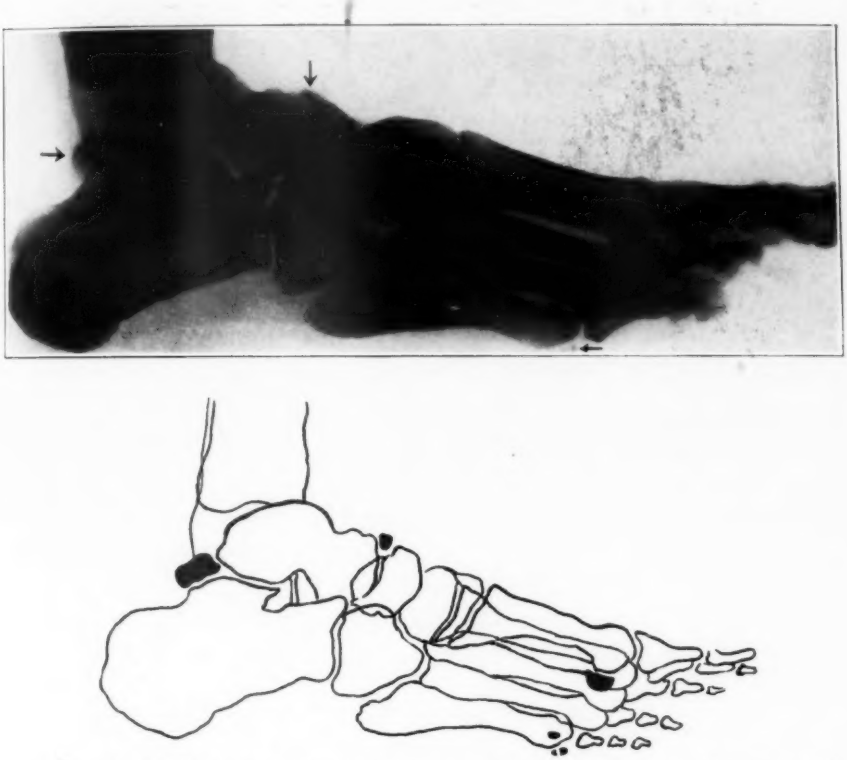

Fig. 9.—Multiple anomalies in a foot: os supranaviculare, os trigonum and congenital division of the fibular sesamoid of the fifth toe.

bone, but not a result of the injury.) Possibly some other cases might have been found if all the roentgenograms had been taken in the oblique plane.

The calcaneonavicular fusion, like many other fusions, may interfere in disarticulation of the foot at the midtarsal joint.

Calcaneonavicular fusion is the most common congenital fusion. Other types have occasionally been observed—calcaneo-astragalar fusion, calcaneocuboid fusion, astragaloscaphoid fusion (astragaloscaphoid bone), scaphoidcuboid fusion. It is unnecessary to discuss these in this

paper, as reference may be made to articles by Leboucq, Anderson, Pfitzner, Illievitz and others. These congenital fusions tend to disaline the statics of the foot and to alter its dynamics.

OS PARACUNEIFORME

This unusual bone, located between the scaphoid and the inner cuneiform bone, on the inner border of the foot, was first noted by

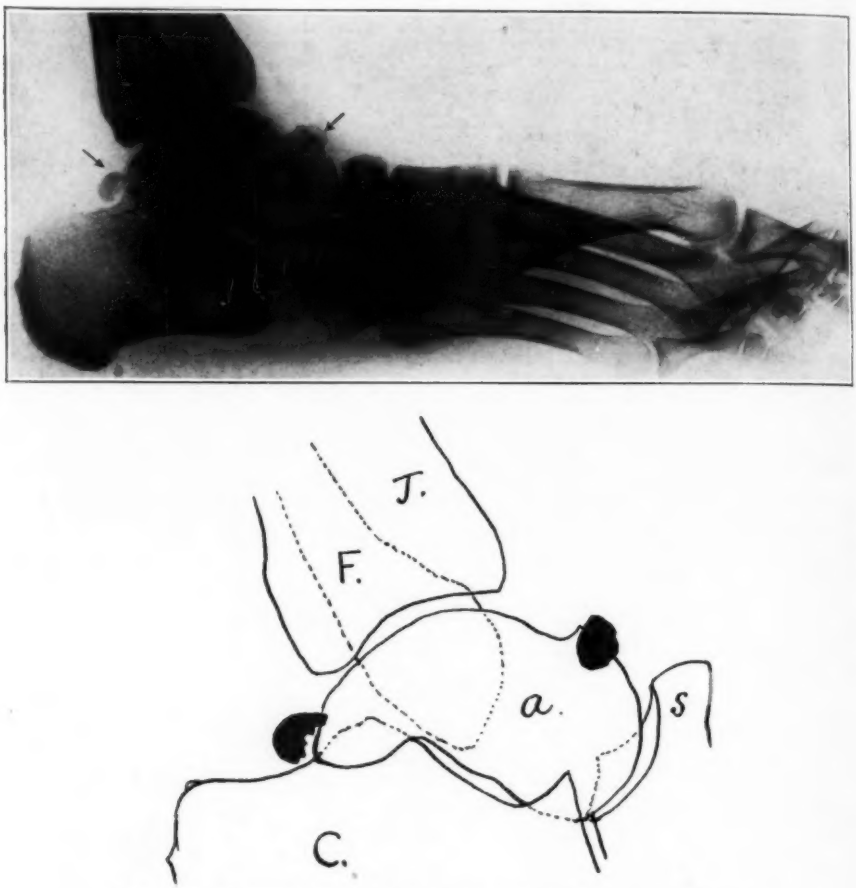

Fig. 10.—Secondary astragalus and a large free os trigonum.

Dwight, who thought it a pathologic formation. He compared it to the bone described by Pfitzner—the pars peronea metatarsalis primi—and said that possibly they were the same. Carlier and Cameron each described clinical cases in which the bone was noted as a projection on the inner border of the foot. In Carlier's patient, a youth of 19, the bone had been present since birth, but it had been growing rapidly in

the few months before examination. The skin was red, and a small bursa was located between the skin and the bone. The bone was slightly movable laterally. A roentgenogram showed this inconstant bone against the inner side of the first cuneiform bone, a thin line of articulation separating them. The bone was removed. In Cameron's case, the bone had an articular facet for the scaphoid; an accessory scaphoid was also present on the same side. We have seen one case in which the bone was present bilaterally.

OS SUPRANAVICULARE

The os supranaviculare is located between the dorsal aspect of the astragalus and scaphoid, usually articulating with the latter, though it may also fuse with the astragalus. It may thus be fused or free. When fused, it may resemble an arthritic exostosis or a trochlear process. Pirie, to whom discovery of this bone is credited, in 1919 described fourteen cases, one of which was bilateral. Pacini, in 1910, Campbell, in 1918, and Wigoder, in 1928, noted this bone. This inconstant bone, if it is one, is to be differentiated from fracture of the superior surface of the scaphoid. We have noted three instances of this bone, two in this series.

SECONDARY ASTRAGALUS

The secondary astragalus is round and located just behind and above the head of the astragalus. It may be fused or free and must be distinguished from fracture, arthritic exostosis, an inflammatory product, as of osteomyelitis, and a trochlear process which is not uncommon on the neck of the astragalus. It is possible that the trochlear process may be a fused secondary astragalus. No functional disturbance is attributed to this bone. In 1921, Bierman described this supernumerary ossicle in a patient with an old osteomyelitis of the tibia. We have seen two cases in this series.

OS SUBTIBIALE

The os subtibiale is an unusual, pea-sized, accessory bone located on the medial aspect of the foot, just below the internal malleolus, anterior to the astragalar facet. From a study of three cases, Bircher believed it to be a sesamoid, and said that it must be differentiated from pathologic calcifications in the ligamentum calcaneotibiale. Grashey, who saw one case, noted the same thing. Hawig and Pfitzner have also noted cases. Gray noted that sesamoid bones may be present, externally or internally, in the tendons turning about the ankle. Lupo said the position and morphology rule out its being a sesamoid bone; he expressed the belief that the line of separation is an articular line.

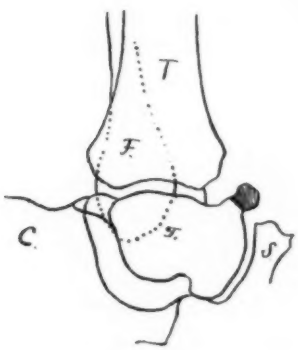

Fig. 11.—Trochlear process of the astragalus or possibly a fused secondary astragalus.

The bone closely resembles a fracture of the internal maleolus. The inconstant bone may be bilaterally present, is smooth and regular, and is to be ruled out as a cause of pain in traumatized ankles. We have seen one case in which a detached osteophytic process in a man suffering from osteo-arthritis of the ankle resembled very much an os subtibiale.

Fairbank has described an unusual epiphysis for the internal malleolus. All his cases have been in children (three cases, two bilateral). In one case he observed fusion of this bone three years after first observation. Whether or not this unusual epiphysis is the os subtibiale is not known. Lamberty and Beclard have also seen this anomaly. Both the os subtibiale and the epiphysis described are to be differentiated from a rare bone located at the posterior part of the sustentaculum tali, the os proprium sustentaculi.

The divided inner cuneiform, the divided cuboid as described by Blandin, and the os intercuneiforme have no functional significance. The secondary cuboid (cuboides secundarius), a bone located in the same general position as the calcaneus secundarius, but in a more plantar and tibialward position, may form a large bony projection in the sole of the foot, as noted by Dwight in the foot of a cadaver. The clinical history was not known. Sutton, Thane, MacAlister, Blandin, Morestin, Gruber and Pfitzner have noted this bone in anatomic specimens. Holland, Bierman and Lilienfeld showed roentgenograms in which they thought the cuboides secundarius was visible. The os unci is present as a bony plantar projection on the third cuneiform and most probably cannot be felt. It is so rare in human beings (normal in cats) that one can only postulate that the enlarged process may be painful on walking. Lilienfeld believed that he saw it once. Holland noted that he observed an ossicle in the region of the peroneal process of the os calcis in relation to the external malleolus.

THE SESAMOIDS

It is not our purpose to discuss the anatomic, anthropologic and physiologic relations of the sesamoids of the foot. This would only lead us astray from a study of the functional derangements of these sesamoids. The reader is referred to the works of Pfitzner, Thilenius, Stieda, Gilette and others for such study.

Osteochondropathy of the sesamoids of the great toe, usually the tibial, is a clinical entity still resting on insecure ground. The etiology is unknown, a lowered resistance of the sesamoids toward mechanical damage in the period of greatest ossification being postulated. Increased static disturbances in a pes planovalgus has been noted in this condition. Meis, Renander, W. Müller and Trèves have described cases. Osteochondropathy is usually found in children, often in association with other epiphyseal disease, such as apophysitis of the heel, Kohler's dis-

ease of the second and third metatarsal head. A few cases have been noted in adults. Clinically, the symptoms are not characteristic—pain under the tibial sesamoid of the great toe, pain on motion of the great toe and on walking and, possibly, limping. Symptoms may not appear until late in the course of the disease. Roentgenologically, there is noticed fragmentation of the tibial sesamoid, usually in two irregular and unequal pieces. A tendency toward increasing fragmentation is seen. In Trèves' patient, a girl aged 19, there was mottling of the tibial sesamoid, suggesting an osteochondritis. The bone was removed but not examined. Two pathologic specimens were examined by two investigators (Meis, Renander), who claimed that the typical picture of osteochondropathy was present. Meis described the pathologic sequence thus—focal necroses of bone trabeculae and marrow, which become confluent, followed by a connective tissue reaction. The resulting frag-

TABLE 3.—*Analysis of the Sesamoids of the Toes*

Division of the inner sesamoid of the great toe noted	72 times
Division of the outer sesamoid	6 times
Second tibial sesamoid noted	34 times
Second fibular sesamoid	Never seen
Third tibial sesamoid noted	4 times
Third fibular sesamoid	Never seen
Fourth tibial sesamoid noted	7 times
Fourth fibular sesamoid	Never seen
Fifth tibial sesamoid noted	163 times
Fifth fibular sesamoid noted	29 times
Interphalangeal sesamoid of the great toe noted	131 times

mentation leads to an appearance of pseudarthrosis. The hyaline cartilage covering remains undisturbed.

This condition is to be differentiated from congenital division of the sesamoids of the great toe and from fracture of these bones. Ossification of these sesamoids takes place about the eighth or ninth year, later according to some authors. Congenital division may be seen then. In our series of 1,000 roentgenograms, 72 showed division of the tibial sesamoid of the great toe, and 6 showed division of the fibular sesamoid. Geist noted such division in 16 of 100 cases; Bizarro in 4 of 100, and Freiberg 1 in 1,000 roentgenograms. Hobart said that no case of division of the fibular sesamoid had ever been reported. The line of division may be transverse or oblique, the fragments being equal or unequal. The line of division is smooth. There may be division into four equal pieces. Sometimes, in addition to the main tibial or fibular sesamoid, one or two smaller sesamoids may be seen, imitating a congenital division. Müller noted that a swelling of the metatarsophalangeal joint may spread apart a congenitally divided sesamoid, imitating fracture. Usually there are no symptoms, but sometimes the patient may complain of pain on the under surface of the

great toe in the region of the tibial sesamoid. This, most probably, is static, and relieved easily by proper conservative treatment. Brugman noted that in some cases of so-called congenital division, an old, long-forgotten fracture of the sesamoid, sustained in childhood, may be present.

Fracture of the sesamoids of the great toe is not common, Bizarro having noted sixty cases up to 1921. Many authors have reported cases—Morian, Mouchet, Jean, Stulz and Fontaine, Hall-Edwards, Schunke, Marx, Hobart, Orr, Koch, Hernaman-Johnson, Müller, Speed, Skillern and Boardman, and others. It is unnecessary to make an analysis in each case to determine whether the condition is congenital division or a fracture. The fracture is usually the result of direct trauma, such as crushing or fall from a height, although some cases are due to indirect trauma. Experimentally, the fracture can be reproduced by forced dorsiflexion and abduction of the great toe. There may be associated fracture of the other bones of the foot, usually of the metatarsals and the phalanges. Fracture of the fibular sesamoid is much rarer, since the tibial sesamoid lies directly beneath the joint. Betocchi has noticed fracture of the fibular sesamoid in cases in which the sesamoid alone is involved by direct injury. Bizarro noted only six cases of fracture of the fibular sesamoid in his review of the literature. Clinically, there is pain under the affected sesamoid, increased on motion of the toe. A limp may be noticed. An association with hallux valgus is seen. On roentgen examination there is seen an unequal division of the affected sesamoid into more or less widely separated fragments, the line of division possibly being serrate. Roentgenograms should be taken with the toe in marked dorsiflexion, the rays being in the frontal plane, after the technic of Müller. Treatment consists of rest, proper physical therapy and proper support. Callus unites the fractured ends, a fact which distinguishes it definitely from congenital division. In some cases, it is necessary to remove the fractured bone. We are definitely in favor of conservative treatment. We have had cases in which operation was indicated for fracture, relieved by paddings and plates; we have also noted that even after the removal of the affected sesamoid in some cases, pain is still present, but is easily relieved by proper support. Luxation of the sesamoids has also been described. This is not uncommonly noticed in marked hallux valgus, in which condition the sesamoids are dislocated outward, the fibular sesamoid being seen in the first intermetatarsal space.

Arthritis of the sesamoids of the great toe is often seen, especially in connection with arthritis of the joint of the great toe. The arthritic exostosis may be joined to a similar exostosis on the second metatarsal. Periostitis of the sesamoids may occur. We have not heard of osteomyelitis or tumor of the sesamoids of the great toe.

D. J. Morton described a backward displacement of the sesamoids of the great toe, and expressed the opinion that there is a definite static effect due to this malposition.

Inconstant sesamoids at the heads of the metatarsals are seen at times. We have never seen the fibular sesamoid on the second, third and fourth metatarsal heads. Stieda described the fourth fibular sesamoid. The tibial sesamoid on the fifth metatarsal head is common, the fibular one less so. Pfitzner's tables of frequency and combinations of the various sesamoids are very interesting. Congenital division has never been described. Pfitzner noted a division of the third fibular sesamoid in a tiger, the third tibial sesamoid being normal. Recently, we noted a congenital division of the fibular sesamoid of the fifth toe into two parts. We have also seen fracture of the second tibial sesamoid, the diagnosis being proved roentgenologically and by microscopic examination of the excised piece.

CONCLUSION

The functional changes due to the inconstant bones of the foot and the sesamoids are not many, but they become important in compensation work, especially in view of the fact that about 75 per cent of feet present such anomalies. The inconstant bones seldom disturb the statics of the foot.

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POSTOPERATIVE PULMONARY ATELECTASIS

OBSERVATIONS ON THE IMPORTANCE OF DIFFERENT TYPES OF BRONCHIAL SECRETION AND ANESTHESIA *

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The importance of pulmonary atelectasis as a postoperative complication has gained increasing recognition during the past few years. At first, attention was focused on the instances of massive collapse, as described by Pasteur [1] (1908) and again by Leopold,[2] who adopted Jackson's designation of "drowned lung," believing the condition to be best described as "post-operative massive pulmonary collapse and drowned lung." This condition is, of course, dramatic in all its phases, but is of relatively infrequent occurrence. However, so-called partial atelectasis is not uncommon—based on my own observations and those of many other observers. In fact, Mastics, Spittler and McNamee [3] stated that the atelectasis accounts for about 70 per cent of all postoperative pulmonary complications.

Strictly speaking, the term partial atelectasis is incorrect. Atelectasis is complete in any given area, but is limited to a greater or lesser portion of the lung according to the magnitude or number of the bronchi that are obstructed. Thus the condition might be considered as "limited atelectasis." Therefore, it would seem advisable to drop the term "partial atelectasis" and to differentiate the various cases of atelectasis by terms descriptive of the areas of the lung involved. Lee and Tucker [4] have offered a classification of the types of atelectasis noted, built on an anatomic basis, namely: (1) massive atelectasis, (2) lobar atelectasis and (3) lobular atelectasis. To this I would add another group, viz., scattered lobular atelectasis, for the following reasons:

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3. Mastics, E. A.; Spittler, F. Q., and McNamee, E. P.: Postoperative Pulmonary Atelectasis, Arch. Surg. **15**:155 (Aug.) 1927.

4. Lee, Q. E., and Tucker, G.: Postoperative Pulmonary Atelectasis, Atlantic M. J. **31**:284 (Feb.) 1928.

It is fairly well agreed that bronchial obstruction plus decreased aeration ability of the lung is a prime cause of postoperative pulmonary atelectasis, and that the obstruction is usually due to retained tracheobronchial secretions. Moreover, limitation of movement of the diaphragm for one cause or another (i. e., air below the diaphragm) greatly aids this process. Numerous other causes have been suggested without any general acceptance of any one of them.

It appears that the rôle of the bronchial secretions either in producing the atelectasis or in determining the specific type of atelectasis which ensues has not been given sufficient consideration. In a study of the action of cough on material in the tracheobronchial tract, Dr. Archibald and myself [5] observed that whereas the usual action of cough is to expel material from the tracheobronchial tree, it may, under certain conditions, actually bring about the opposite result, that is, drive material deeper. Moreover, it was noted that the degree of penetration of the material into the smaller ramifications of the tracheobronchial tree was in direct proportion to the viscosity of the material in question, that is, the less viscid the material, the greater was the penetration and the greater the possibility of dispersion.

In the cases of postoperative pulmonary atelectasis apparently due to bronchial obstruction by mucous secretion, I had the opportunity to observe carefully different types of secretion. The usual type of secretion consists of a thick viscid material, not necessarily present in large amounts, and broken up with difficulty. On bronchoscopic examination, this material is found to plug a bronchial orifice, atelectasis occurring distal to the plug. If the material is slightly less viscid, one or more smaller bronchi may become plugged, and as the material found is again less viscid, smaller bronchi still are seen to be filled or plugged, and the possibility of obstruction in more than one bronchus increases. Finally, when one notes a secretion of almost watery consistency, then not only bronchial plugging, but also bronchial filling, may occur, and one obtains clinically the condition which has been spoken of as "drowned lung" (Leopold [2]).

The experiments consisted in introducing intratracheally into animals, sputum that had been impregnated with iodized poppy seed oil 40 per cent, inducing controlled cough, and making roentgenographic observations. Thick, viscid sputum did not penetrate deeply, did not break up and was arrested at the orifices of the larger bronchi (fig. 1). Thin sputum (a sputum-iodized oil emulsion) penetrated deeply, filled the bronchi and was widely dispersed (fig. 2). In the various experiments, all factors were identical except the type of sputum introduced.

5. Archibald, E., and Brown, A. L.: Cough—Its Action on Material in the Tracheobronchial Tract: Experimental Study, Arch. Surg. **16**:322 (Jan.) 1928.

Clinically, I have frequently observed that thick, viscid sputum may plug larger bronchi and produce a postoperative lobular atelectasis. A typical case is reported (case 1, fig. 3).

CASE 1.—The diagnosis before bronchoscopy was atelectasis of a portion of the right lower lobe; after bronchoscopy, atelectasis of two tertiary lobules, right lower lobe.

A 10 mm. Bruning's bronchoscope was inserted. A small amount of thin mucous material was found in the trachea. The left primary bronchus was clear;

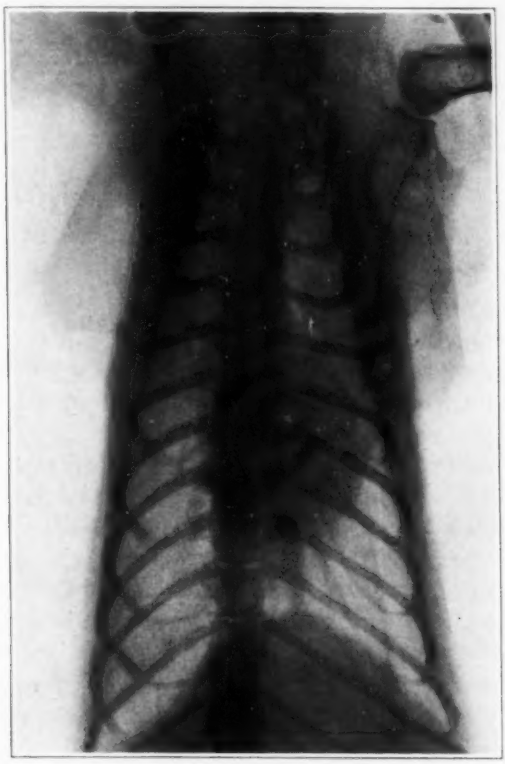

Fig. 1 (cat 9).—In the cardiac region is seen an area of increased density corresponding to a mass of sputum-impregnated iodized oil, which had been injected intratracheally after cough had been induced. The mass is intact and has only penetrated the larger bronchi. Repeated induced coughs failed to disintegrate the mass or drive it further in.

no blocks were noted. At a distance of 37 cm. from the mouth down the right primary bronchus and into the anterior secondary bronchus, two posterolateral tertiary bronchi were noted to have their orifices completely blocked by small plugs of thick, tenacious sputum. The patient was asked to take deep breaths, but these plugs were immovable, whereas the thin mucous secretion of the bronchi moved in and out with respiration. The entire area was sprayed with 10 per cent cocaine and 1:1,000 solution of epinephrine, equal parts. The aspirator was

applied directly to these plugs of mucus, and each was removed. The air was seen to enter the bronchi involved. The orifices of each were then touched with the mixture of cocaine and epinephrine, and before withdrawal were seen to be about one third larger than at the beginning of the procedure. After withdrawal of the bronchoscope, it was noted that the physical signs had changed, and that respiration was much easier.

Roentgenograms taken immediately before and after bronchoscopy showed clearing of the atelectatic area after bronchoscopy.

Fig. 2 (cat 10).—After induced cough, sputum-iodized oil emulsion is seen dispersed and filling the larger and smaller bronchi.

Case 2 is a typical illustration of what may occur when the consistency of the sputum is much less viscid. In this case there was observed a dispersion effect with filling of numerous scattered bronchi and bronchioles; directly comparable, it is believed, to the experimental observations previously reported.

Case 2.—The diagnosis before bronchoscopy was atelectasis of the right lung; after bronchoscopy, atelectasis of the right lung and scattered atelectasis.

The large bronchoscope was inserted. About 30 cc. of fairly tenacious sputum was aspirated from the trachea and primary bronchi, especially on the right side.

No definite plugs were noted. The patient breathed more freely after the operation and was markedly improved symptomatically.

Roentgenograms taken immediately before and after bronchoscopy showed some clearing after bronchoscopic aspiration (fig. 4). Roentgenograms taken twenty-four hours later showed marked clearing throughout.

Thus I have shown clinically that thick, tenacious sputum may plug a larger bronchus without interfering with the remainder of the tracheobronchial tree, and that a marked dispersion effect with filling of numerous widely scattered bronchi and bronchioles may occur when rather thin sputum is present. Intermediate degrees of dispersion and

Fig. 3 (case 1).—*A*, roentgenogram taken immediately before bronchoscopy showing a triangular area of increased density at the base of the right lung. There was retraction of the ribs on the right and the heart and mediastinal contents were drawn slightly toward the right. At bronchoscopy, the bronchus in this area of increased density was found to be occluded by a thick tenacious plug. *B*, taken after bronchoscopy showing marked clearing of the triangular shadow at the base of the right lung and widening of the interspaces. The heart and mediastinal contents have swung back toward the left. This followed the bronchoscopic removal of the thick tenacious mucous plug filling the bronchus to the area involved.

plugging of a few or many bronchi in other clinical examples were obviously to be expected, and this has been noted repeatedly; the cases quoted herewith fall, respectively, toward each end of the scale.

INFLUENCE OF TYPE OF ANESTHESIA

It has been my privilege to observe the course of postoperative pulmonary complications following practically all types of anesthetics. The majority of the operations were performed under subarachnoid block. Likewise, the greatest number of cases in which postoperative pulmonary atelectasis were observed were those in which spinal anesthesia had been employed. While the series is numerically too small to give definite statistics for the incidence of this complication following the various types of anesthesia, nevertheless, the impression gained thus far is definitely that the incidence of pulmonary atelectasis is greater follow-

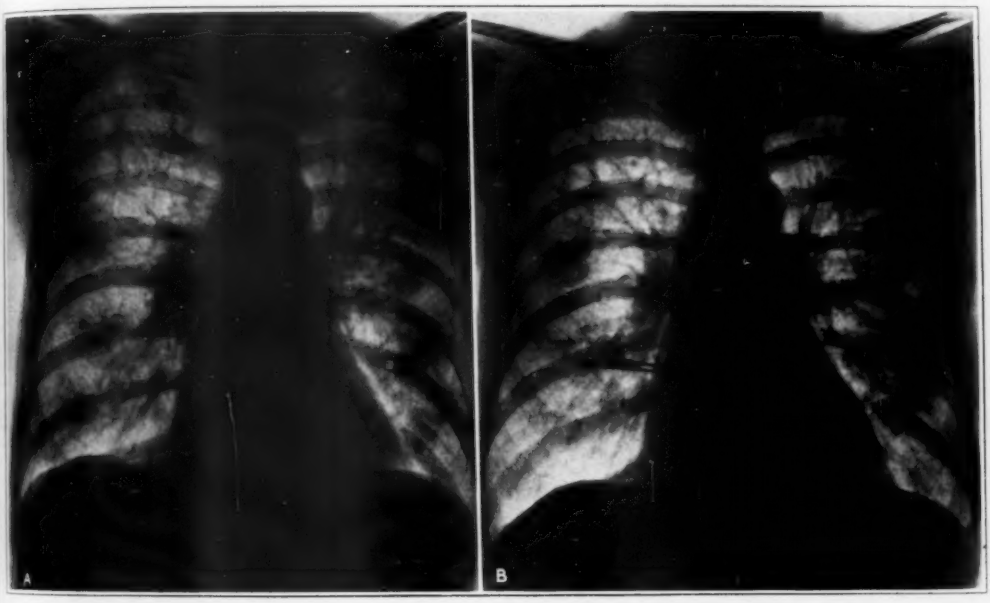

Fig. 4 (case 2).—*A*, roentgenogram taken before bronchoscopy showing diffuse scattered areas of increased density throughout both lobes. At bronchoscopy, a large amount of semiviscid material was found in all the major bronchi. *B*, after bronchoscopy, during which procedure 30 cc. of semiviscid material was aspirated from the primary bronchi, showing slight general clearing most marked on the right.

ing spinal anesthesia than following any form of inhalation or regional anesthetic. This impression holds regardless of the type of operation undertaken.

At first thought, one would imagine the opposite to be true, that postoperative pulmonary atelectasis would occur more frequently following inhalation anesthesia. But on closer consideration, several reasons are noted why spinal anesthesia might predispose to this complication.

First, spinal anesthesia definitely inhibits the depth and force of respiratory movements, not only during the operation itself, but for a considerable period thereafter. It is these respiratory movements (both intrinsic and extrinsic) which tend to rid the tracheobronchial tree of foreign matter or secretions. Second, the normal viscosity of the secretions of the tracheobronchial tree appears to be increased, i. e., the material is more tenacious following spinal anesthesia. Third, following operation under spinal anesthesia the patient tends to remain relatively quiet for a number of hours. One has, then, a more tenacious sputum and decreased or impaired factors that might tend to free the tracheobronchial tree of this material. The increased possibility for this material to obstruct or plug a bronchus and the subsequent development of atelectasis appear reasonable.

SUMMARY

1. The importance of the bronchial secretions in producing postoperative atelectasis and in determining the specific type of atelectasis which ensues is stressed. Experimental and clinical observations are compared, and are found to agree. Thick, tenacious sputpum is noted to plug the larger bronchi, whereas thinner sputum tends to greater dispersion and a blocking of the finer bronchi and bronchioles, thereby producing a scattered lobular atelectasis.

2. The impression is gained that spinal anesthesia predisposes to postoperative pulmonary atelectasis.

PERITONITIS

AN EXPERIMENTAL STUDY OF HEALING IN THE PERITONEUM AND THE THERAPEUTIC EFFECT OF AMNIOTIC FLUID CONCENTRATE *

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The reaction of the peritoneum to trauma and the resistance of the peritoneum to bacterial invasion have always been subjects for study and speculation. Notwithstanding the countless investigations and clinical observations of past years, there is yet much to be learned.

It is generally understood that aseptic trauma to the peritoneum gives rise to a reaction tending to produce healing with the formation of adhesions of scar tissue of greater or less degree. If in addition to trauma there is bacterial contamination of the peritoneum, the healing process is complicated by infection or peritonitis. In the broadest sense, the term peritonitis may include the reaction of the peritoneum to any injury, whether it be simple trauma, chemical irritation or infection. That mere contamination of the normal peritoneum with living pathogenic bacteria does not necessarily produce fatal peritonitis is a matter of common knowledge. Dogs often will tolerate massive intraperitoneal injection of living staphylococci, streptococci or colon bacilli without apparent damage. If, however, the peritoneum is injured or contaminated with gross débris in addition to bacteria, the tendency to fatal peritonitis is greatly increased.

These facts offer some explanation for the variable and confusing clinical observations concerning the development and course of peritonitis in the human subject. Obviously, however, there are many other factors poorly understood. Why should healing following a minor operative trauma in the abdomen occur with the formation of damaging peritoneal adhesions in one patient while another patient with extensive peritoneal exudation around an acutely inflamed appendix recovers from operation without adhesions? It is obvious that the formation of inflammatory adhesions is a necessary protective mechanism in the reaction of the peritoneum to severe injury, to infection or to surgical

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* Amniotic fluid concentrate is a filtered fractionated sterile preparation of bovine amniotic fluid, concentrated 5 to 1 and prepared for clinical trial by the Eli Lilly Research Laboratory.

intervention. For a favorable result, it is essential that any peritoneal inflammation be walled off promptly, and that a vigorous reaction manifest itself early. It is equally true, however, that restoration to normality depends on the prompt resolution of these areas. It is with the hope that my experimental observations will cast some light on the factors which accelerate these reactions that this paper is written.

EXPERIMENTAL OBSERVATIONS

My attention was first called to this subject by the work of Johnson,[1] who conceived the idea that amniotic fluid might be effective in the prevention of postoperative abdominal adhesions. With the aid of Warren,[2] he conducted experiments on guinea-pigs, using first amniotic fluid obtained at cesarean section and later a concentrate prepared from bovine amniotic fluid. Their observations on guinea-pigs subjected to laparotomy and trauma to the bowel clearly indicated that

TABLE 1.—*Guinea-Pigs: Trauma to Peritoneum Under Sterile Precautions Showing the Effect of the Intraperitoneal Injection of Amniotic Fluid and Other Agents*

Substance Used	Number of Pigs	Peritoneal Adhesions				
		None	Slight	Moderate	Dense	Died
None (control)	121	7	13	17	59	25
Horse serum	13	..	4	2	7	..
Papaine	30	4	1	12	7	6
Dextrose, 50 per cent	35	10	5	10	5	5
Allantoic fluid	38	..	2	6	25	5
Amniotic fluid concentrate	396	92	46	98	117	43

the intraperitoneal use of amniotic fluid resulted in better healing in the treated series, fewer adhesions and a lower mortality than in a similar series of untreated controls. In checking their results, I have observed a large series of experimental animals, approximately 600 guinea-pigs and 160 dogs.

EXPERIMENTS ON GUINEA-PIGS: TRAUMA TO PERITONEUM

The guinea-pigs in table 1 were subjected to laparotomy with a technic as nearly aseptic as possible. The small intestine was picked up with blunt instruments. A uniform degree of trauma was inflicted on the peritoneal coat of the bowel and on a definite area of the parietal peritoneum. In the treated animals, the fluid in question was injected intraperitoneally during the closure. The animals were reopened for observation in three weeks.

1. Johnson, H. L.: Observations on the Prevention of Postoperative Peritonitis and Abdominal Adhesions, Surg. Gynec. Obst. **45**:612-619 (Nov.) 1927.

2. Warren, Shields: The Effects of Amniotic Fluid on Serous Surfaces, Arch. Path. **6**:860-866 (Nov.) 1928.

The results obtained are not so striking as those reported by Warren, but there is obviously the same tendency toward better healing in the treated animals. The death rate in the treated series is too high, owing to the presence of a virulent respiratory infection in the stock of small animals during a part of the period necessary for the investigation. In the observations on these animals, the personal equation was minimized and favoritism was prevented by the making and recording of the observations before it was determined to which group the animal belonged. Adhesions were called dense when the intestines were so matted by fibrous adhesions that separation could be accomplished only by gross damage to the bowel. They were called moderate when separation produced only a reasonable amount of raw oozing surface. Slight adhesions were filmy veils which separated easily and without damage. I was impressed by the fact that the adhesions found in the amniotic fluid series were characteristically filmy and easily broken. Though many of these animals were credited with dense adhesions, they were seldom of the firm, fibrous consistency which the controls displayed.

Numerous animals not included in the table were utilized in the attempt to determine the nature of this action and what might be the best preparation of amniotic fluid to employ. The one which seemed to give the most favorable reaction was amniotic fluid concentrate. This product is a filtered fractionated sterile preparation of bovine amniotic fluid concentrated 5 to 1 and prepared for clinical trial by the Eli Lilly Research Laboratory. The fractionation disposes of the larger protein molecules and also of the smaller nitrogenous molecules. The final product is a clear, isotonic straw-colored solution of polypeptides containing 1:20,000 methyolate as an added factor for sterility. It is stable, nontoxic on intravenous injection into animals and gives no anaphylactic reactions. This preparation is the one on which this report is based. The quantities which the guinea-pigs received varied from 4 to 10 cc. The larger quantities, although not harmful, appeared to be unnecessary. Warren in attempting to explain the therapeutic action of amniotic fluid called attention to two factors: first, its tendency to lessen the time of oozing when placed on injured surfaces; second, a lubricating action due to the delayed absorption of the fluid. The first factor I have noted. I regard it as the hemostatic action common to many protein substances. The second may be a factor, but certainly this interpretation does not explain my observations. When observed from forty-eight to ninety-six hours postoperatively, the peritoneums of the treated animals looked different from that of the control. There was in the former a definite increase in the reaction to injury. Hyperemia and exudation were both more pronounced. Microscopic study revealed that the exudate was not merely the unabsorbed amniotic fluid. In fact, observations following

simple intraperitoneal injection into the normal peritoneum showed that the bulk of the fluid was absorbed well within the interval mentioned.

The other substances listed in table 1 were tested chiefly for the purpose of comparative study. Among them dextrose [3] and papain [4] have been reported as agents tending to reduce the formation of peritoneal adhesions. All of these substances seem to produce in the traumatized peritoneum a reaction similar to that described for amniotic fluid concentrate. The manner in which they differ and the evaluation of this information will be discussed later.

EXPERIMENTS ON DOGS: TRAUMA TO PERITONEUM

In order to study more accurately the mechanism of this therapeutic effect, I have made numerous observations on dogs. The animals described in table 2 were subjected to laparotomy and trauma to the vesical peritoneum under sterile precautions. The technic which gave

TABLE 2.—*Dogs: Aseptic Trauma to Peritoneum Showing Therapeutic Effect of Amniotic Fluid Concentrate*

Substance Used	Number of Dogs	Peritoneal Adhesions				Death from Peritonitis or Obstruction
		None	Slight	Moderate	Dense	
None (control)	22	0	2	3	10	7
Papain solution 1:40,000	5	0	0	2	2	1
Horse serum	8	0	2	3	0	3
Autoclaved amniotic fluid	6	0	0	3	1	2
Dextrose solution, 50%	9	2	3	2	0	2
Dextrose, 25%, in amniotic fluid	4	2	2	0	0	0
Amniotic fluid concentrate	22	5	10	5	1	1

the most definite result was as follows: Under ether anesthesia the abdomen was opened through a low midline incision. The entire small intestine was pulled up. Trauma was inflicted in two definite areas. The peritoneal coat of the upper jejunum was abraded by scraping with the sharp blade of a scalpel to produce a raw oozing surface for a distance of from 10 to 12 inches. The same procedure was carried out in the lower part of the ileum. Care was taken not to cut through into the muscular coat. In some instances, the same result was obtained by brisk rubbing with gauze sponges. In a few instances the liver and other peritoneal surfaces also received trauma. The entire series, however, may be tabulated as a group, because each animal was checked with a control. In each of the animals receiving the various fluids, a small amount of the agent in question was placed directly on the oozing surfaces, and the remainder of a 50 cc. quantity was injected freely into the peritoneal cavity during the closure. The animals were given

3. Mann, F. C.: Personal communication.

4. Kubota, Takashi: The Prevention of Peritoneal Adhesions, Japan M. World **2**:226 (Aug.) 1922.

reasonable postoperative care, but were allowed to run free in pens taking food and water ad libitum. The postoperative appearance of the treated animals was uniformly better and their convalescence was obviously smoother than that of the controls.

In analyzing the results of these experiments, there are several points to be considered. Many of the animals in table 2 were followed for several months and opened repeatedly to study the mechanism of healing. The observations led me to conclude that amniotic fluid concentrate, when placed in contact with traumatized peritoneal surfaces, acts by stimulating the normal processes of repair. When the untreated control is reopened for observation at forty-eight or ninety-six hours, one finds hyperemia and localized exudation with all abraded surfaces adherent to one another. The treated animal shows a slightly

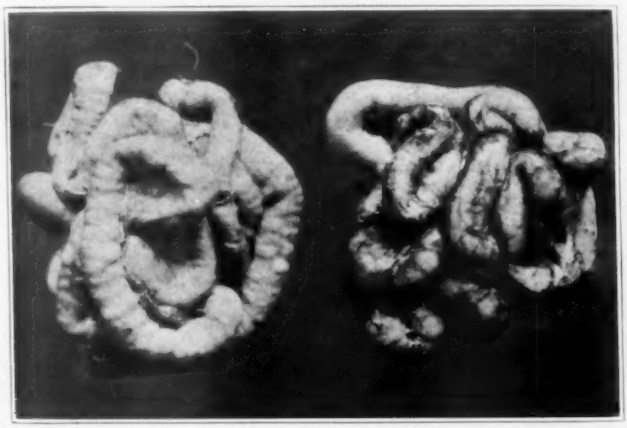

Fig. 1.—Appearance of small intestine of two dogs after repeated laparotomies. At the first operation the visceral peritoneum was traumatized to the same degree in each case. At three subsequent laparotomies, the intervals being approximately twenty-one days, all adhesions were separated. *A* (represented by the intestine at the left) received 25 cc. of amniotic fluid concentrate intraperitoneally following each operation; *B* (right) served as a control.

more marked hyperemia and a great increase in the amount of exudate, which contains serum, fibrin and leukocytes, in large numbers. There is a tendency for the abraded surfaces to float free in the exudate, with an obvious facilitation of healing.

After ninety-six hours, the reaction has passed through its maximum, and the exudate becomes a film or meshwork of fibrin in which repair of the traumatized tissue and regrowth of the endothelial covering takes place rapidly. Though the difference is one of degree rather than of type, the healing mechanism under these conditions is decidedly better than that displayed by the untreated control, in which the traumatized surfaces adhere and heal by the formation of firm adhesions.

This difference is noticeable whether observation is made in fifteen or thirty days or several months. In the animals that were observed repeatedly, the routine practice was to break down the adhesions. The controls were then closed without further interference, and the treated animals received reinjection of the therapeutic agent. There was a constant tendency for the animals receiving the amniotic fluid concentrate to show progressively better healing and fewer adhesions with each exploration. In the controls the condition of the peritoneum became progressively worse under this treatment, a result which is entirely in accord with surgical experience. The bulk of the data in table 2 is taken from observations made at exploration six weeks after the original trauma. As stated before, however, some of these animals

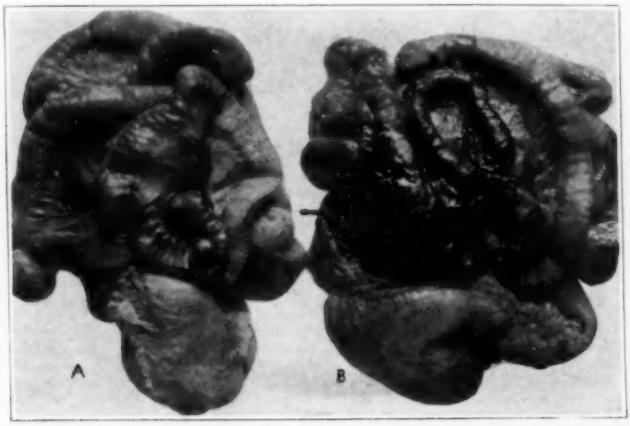

Fig. 2.—Appearance of gastro-intestinal tracts of two dogs, fifteen days after intestinal anastomosis. *A* received 50 cc. of amniotic fluid concentrate intraperitoneally. *B* served as a control.

were explored repeatedly. Complete protocols were kept, but to record them in detail would be laborious and futile. The table constitutes the briefest possible analysis, and, since each treated animal was paralleled with a control, comparative study of the results so tabulated should give an accurate evaluation. The recording of a large control series also compensates for the known fact that there is considerable individual variation in the degree to which adhesions form in the experimental animal.

Realizing that peritoneal adhesions in the experimental animal are not produced with any regularity by any of the numerous minor factors to which adhesions in human subjects are often attributed, my associates and I made the traumatizing procedures in these animals quite severe. As evidence of that fact table 2 shows that adhesions were present in

the entire control series, and that in 75 per cent the result was dense adhesions or death from obstruction or from peritonitis. In contrast, observations on the series receiving amniotic fluid concentrate showed 70 per cent of the dogs with slight or no adhesions. The other substances tabulated in table 2 were employed chiefly to assist in studying the nature and mechanism of this therapeutic effect. A full discussion of these points will be undertaken in a later paragraph.

EXPERIMENTS ON PERITONITIS

In the observations on animals treated with amniotic fluid concentrate as described, I was impressed with the low death rate from peritonitis as compared to that of the controls. In order to check this effect more closely, I conducted a number of experiments as follows: Dogs were subjected to peritoneal trauma and, following the closure, to an intraperitoneal injection of virulent pathogenic bacteria,[5] one series

TABLE 3.—*Dogs Subjected to Peritoneal Trauma and Bacterial Contamination*

Bacteria	Substance Used	Number of Animals	Died of Peritonitis
Staphylococcus (hemolytic)	None (control)	8	6
	Dextrose, 50%	4	4
	Dextrose, 25%, in amniotic fluid	6	6
	Amniotic fluid concentrate	8	2
Streptococcus	None (control)	6	4
	Amniotic fluid concentrate	6	0
Bacillus coli	None (control)	5	2
	Amniotic fluid concentrate	5	0

receiving staphylococcus, another streptococcus and another *Bacillus coli*. In each case 20 cc. of a heavy suspension was injected. The treated series received exactly the same dose as the controls. Results are given in table 3.

The experiments presented in table 3 constitute a crucial test of this amniotic fluid concentrate preparation. On first thought it would seem dangerous to inoculate the peritoneum with a foreign protein substance in the presence of heavy bacterial contamination. The results, however, are strikingly favorable. Though the series is perhaps too small to be absolutely convincing, it does appear that the reaction by which amniotic fluid stimulates healing is likewise effective in checking the development of fatal peritonitis. It is also striking that dextrose solution, though it exerts a favorable action on healing in the absence of contamination, seemed to hasten the death of the animals contaminated with staphylococci.

5. Bacterial cultures prepared by Edith Haynes, Ph.D., bacteriologist for Indiana University hospitals.

In another short series of animals, I noted the effect of amniotic fluid concentrate on peritoneal healing following surgical procedures on the intestines.

The operations reported in table 4 were conducted with good technic. Intestinal clamps were not employed, however, and the contamination was that to be expected under such conditions. Observations were made in approximately thirty days. Healing was uniformly better in the treated animals. In the series with intestinal anastomosis in addition to trauma, the high death rate of the controls is significant.

MECHANISM OF THERAPEUTIC ACTION

Amniotic fluid concentrate does not act as a lytic agent. It has no power to digest or dissolve adhesions. Neither does it interfere in any way with the normal "walling off" of inflammatory areas in the peritoneum. When these surfaces are severely damaged by trauma or infection, formation of adhesions is inevitable, but in any case the scar

TABLE 4.—*Intestinal Surgery on Dogs*

	Substance Used	Number of Animals	Good Healing	Dense Adhesions	Died of Peritonitis
Gastro-enterostomy	None (control)	5	2	2	1
	Amniotic fluid concentrate	5	4	1	0
Intestinal anastomosis	None (control)	12	6	6	0
	Amniotic fluid concentrate	12	10	2	0
Intestinal anastomosis plus trauma to intestine	None (control)	5	0	2	3
	Amniotic fluid concentrate	5	3	2	0

is less dense and damaging in the treated animal. It is elementary knowledge that accelerated healing and epithelization minimize cutaneous scarring. My evidence indicates that this agent acts in the peritoneum by accelerating the normal reaction. I am inclined to consider two possible explanations. First, the substance may contain the growth-promoting agents which are known to exist in embryonal juices and may in this way stimulate regrowth, especially that of endothelial cells. Second, it may be considered a mild irritant which exerts a chemotactic action and stimulates the peritoneum to a more rapid and more powerful defense reaction, thereby in a nonspecific fashion intensifying the local factors of immunity and repair.

In support of this second explanation is the fact that the other substances tested are mildly irritating and bring about a similar reaction in the peritoneum. Among these, 50 per cent dextrose is the most effective in the prevention of adhesions, but its dangers and unfavorable possibilities are obvious. Papain and horse serum likewise are of experimental interest only. I have employed them with the idea of making a comparative study. They are nonspecific, and their action is similar though not as effective as that of amniotic fluid.

David [6] demonstrated that a well formed plastic exudate is of itself a factor of immunity in the peritoneum. By the intraperitoneal injection of dilute turpentine emulsion into dogs, he was able under certain conditions to produce an exudate which inhibited the absorption of bacteria and of toxins introduced later. Rankin and Bargen [7] demonstrated the therapeutic value of preoperative intraperitoneal vaccination in patients requiring resection of the colon for malignancy. In a series of sixty cases in which intraperitoneal injections were given with a mixed vaccine of colon bacilli and streptococci, the operation being performed two days following the last injection, there was a mortality of 5 per cent, in contrast to a mortality of 23 per cent in the control series. They further stated that postoperative convalescence was noticeably smoother in the treated cases.

COMMENT

The foregoing discussion indicates that amniotic fluid concentrate may act nonspecifically as a "vaccine" to the peritoneum. I have no evidence that it acts also as an embryonal juice, though this may be possible. In any event, I believe it to be unique in the effectiveness with which it facilitates peritoneal immunity and repair. Whether or not there is any relationship between its source and its therapeutic action is a matter of little consequence.

CLINICAL APPLICATIONS

To formulate clinical conclusions purely on the basis of experimental evidence is poor practice. Amniotic fluid concentrate, however, has already been subjected to clinical trial. Johnson [8] and others, including myself, have used it intraperitoneally in all types of abdominal operations. Though no conclusive observations can be made, it is noticeably apparent that these patients tend to enjoy a smooth postoperative course, and that there have been no indications of unfavorable action. This statement is emphasized because of a tendency on the part of surgeons to look unfavorably on any agent that is reported to prevent abdominal adhesions. As previously indicated, I am not unaware that formation of peritoneal adhesions is the one mechanism that makes abdominal operations possible. I maintain, however, that a favorable end-result depends on the prompt resolution of such areas. All my observations,

6. David, V. C.: Peritonitis: Experimental Study, Surg. Gynec. Obst. **45**: 287-293 (Sept.) 1927. David, V. C., and Sparks, J. L.: The Peritoneum as Related to Peritonitis, Ann. Surg. **88**:672-677 (Oct.) 1928.

7. Rankin, F. W., and Bargen, J. A.: Carcinoma of the Colon: Intraperitoneal Vaccination by Mixed Vaccine of Colon Bacilli and Streptococci, Arch. Surg. **19**:906-914 (Nov.) 1929.

8. Johnson, Herbert L.: Personal communication to the author.

both experimental and clinical, indicate that amniotic fluid concentrate acts merely by accelerating both the inflammatory response and the resolution thereof. Though large quantities of the fluid may be used, from 50 to 100 cc. in the human abdomen is probably sufficient.

My experimental studies indicate that the use of amniotic fluid is indicated especially in two types of abdominal cases: (1) those in which inflammatory adhesions are encountered and broken up, leaving extensive raw surfaces; (2) any cases in which there may be contamination, notably in gastro-intestinal operations. I see absolutely no indication that the substance could exert a beneficial action when a far advanced or generalized peritonitis is encountered at the time of operation. There is no evidence that its use under these conditions is harmful. In any case, its therapeutic value must be considered that of a prophylactic agent.

CONCLUSIONS

1. Experimental studies indicate that amniotic fluid concentrate when injected into the traumatized peritoneum produces a reaction stimulating the normal processes of repair and thus minimizing postoperative adhesions.

2. In the presence of contamination, this reaction likewise inhibits the development of fatal peritonitis. But there is no evidence that it can exert a beneficial action when a far advanced peritonitis is encountered at operation.

3. These observations indicate a therapeutic value which has already been substantiated to a limited extent by clinical trial.

23 East Ohio Street.

GASEOUS PERICHOLECYSTITIS WITH CHOLECYSTITIS AND CHOLELITHIASIS *

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Gas bacillus infection of the liver and biliary tract has been reported many times. In a perusal of the available literature, I have not found a case in which gas formation around the gallbladder was noted during life. Kirchmayr reported an interesting case of gas bacillus infection within the gallbladder, the walls of which showed emphysematous blebs.[1]

In the case presented, gas in increasing volume was demonstrated both clinically and roentgenologically in relation to the gallbladder. The gas present at the time of operation was proved by culture to be due to an unusual gas bacillus resembling the *Bacillus welchii*.[2]

In all case reports of emphysema of the liver, the presence of gas was first noted post mortem. It is interesting that invariably there was an associated chronic cholangeitis, usually with cholelithiasis.

From a microscopic study of the liver and biliary system in cases of "Schaumleber," Stolz [3] concluded that the invasion of the bile ducts and gallbladder by the gas bacillus was terminal and the gas formation a postmortem feature. Hintze,[4] Kerschensteiner,[5] Welch [2] and others are of the opinion that the invasion and localization of gas producers in the bile ducts and periacinal areas of the liver may occur during life; the production of gas begins only after cessation of the circulation.

Bacillus aerogenes-capsulatus is frequently present in the bowel. It may be present in the circulation without causing symptoms until some intercurrent necrotic or inflammatory lesion develops which forms a favorable nidus for its growth. A necrotic area being deprived of or limited in its supply of well oxygenated blood may determine such localization.

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* From the University of Colorado School of Medicine and Hospitals

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1. Kirchmayr: Centralbl. f. Chir. **52**:1522, 1925.

2. Welch, W. H., and Nutall, C. H. F.: Bull. Johns Hopkins Hosp. **3**:81, 1891.

3. Stolz: Arch. f. Path. **165**:90, 1901.

4. Hintze: München. med. Wchnschr. 1895, no. 10, p. 290.

5. Kerschensteiner: Deutsches Arch. f. klin. Med. **69**:38, 1900.

The liver eliminates bacteria from the general and the portal circulation through the biliary ducts.[6] This function is of prime importance for the maintenance of health. It may become an equally important etiologic factor in diseases of the hepatic system. Investigations by different observers show that a variety of bacteria may be present in the liver and bile for an indefinite period without clinical manifestations of their presence. The liver and bile must possess the power to modify or control the virulence of bacteria.

An increase in alkalinity of the bile has a marked inhibitory and possibly a bactericidal effect.[7] This may explain why bile may be sterile, whereas the walls of the gallbladder and biliary ducts with the pericystic and periductal fibrous tissues and the contiguous liver cells retain and manifest bacterial infection.

Any severe or fatal illness which diminishes the secretion or alters the character of bile, any condition reducing the contractility of the gallbladder [8] or which causes biliary stasis,[9] favors infection of the bile. These factors can be held to account for descending as well as for ascending biliary infection.

The routes of infection to the gallbladder and bile passages have recently attracted renewed attention of investigators, notably Graham [10] and his co-workers, Peterman and Priest.[11] It is important to know the route of invasion in order to understand diseases of the hepatic system. Usually when the patient with hepatic disease seeks medical aid, the avenues of invasion are so intimately and inseparably associated that the disease is presented as an overlapping and confusing pathologic complex.

Systemic infection with gas producers may follow even minor injuries to the surfaces of the body, or minute or massive perforations of the hollow viscera. Lesions of the bowels, ulcers, contusions, strangulation or obstruction which increase permeability of the wall without solution of continuity may be the site of inoculation. There may be no visible point of inoculation.[12] Gas bacillus infection of the gastrointestinal tract and related systems is usually an autoinfection.

The routes of invasion of the gallbladder and bile passages may be:

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6. Fütterer: Berl. klin. Wchnschr. **36**:58, 1899.
7. Beckmann, K.: München med. Wchnschr. **75**:2042, 1928.
8. Gilbert and Gironde: Centralbl. f. Bact. **9**:413, 1891.
9. Ehret and Stolz: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **7**:8, 1901.
10. Graham, E. A.: Surg. Gynec. Obst. **26**:521, 1918.
11. Peterman, M. G.; Priest, W. S., and Graham, E. A.: The Association of Hepatitis with Experimental Cholecystitis and Its Bearing on the Pathogenesis of Cholecystitis in the Human, Arch. Surg. **2**:92 (Jan.) 1921.
12. Welch, W. H., and Flexner, S.: J. Exper. Med. **1**:5, 1896.

(*a*) Arterial: A part of a general sepsis,[13] from remote foci, as proved by the work of Rosenow;[14] bacterial emboli in the subepithelial or submucous tissue of the gallbladder.[15]

(*b*) Venous: Thrombophlebitis, thrombosis of the portal vein or its branches, a result of filtration of bacteria from the general, splenic or portal circulation by the liver cells through bile ducts.[16]

(*c*) Lymphatic: From the liver, from organs contiguous to or in physiologic relation with the liver. Graham[11] showed the lymphatic route as probably the most frequent, corroborating the studies of other workers who found the greatest and most constant evidence of infection in the periportal, periductal and perivesicular fibrous tissues, which conduct the lymphatic channels.

(*d*) Adhesions between the bowel, liver and gallbladder: Adhesions, primarily a protective inflammatory reaction, become a bridge across which infections may travel in both directions. The same features obtain between the undersurface of the liver, the sulcus of the gallbladder and the gallbladder proper.

(*e*) Direct extension from the liver by continuity.

(*f*) Bile stream infection: Ascending from the duodenum, descending from the hepatic ducts.

REPORT OF CASE

History.—J. B. L., a man, aged 62, was admitted as an ambulant patient to the medical service of Dr. C. T. Burnett on March 21, 1929, complaining of pain in the upper part of the abdomen. He had had a similar attack of three hours' duration three weeks before; otherwise he was well. Five days before admission, following a heavy meal, he was seized with sudden agonizing pain in the upper right quadrant of the abdomen. The pain radiated to the back and to the right shoulder, and persisted for four and one-half days. He was nauseated and vomited undigested food and bile. Jaundice was noted on the second day, which began to fade on the day before admission.

Examination.—On physical examination the patient was found to be robust and did not appear ill. The temperature was 99 F., the pulse rate 92 and the respiratory rate 22. The skin and sclera were jaundiced. The right upper quadrant of the abdomen was rigid and tender below the right costal border. No mass was palpable. The heart was normal. The systolic blood pressure was 136 and the diastolic 76. The blood count was: red blood cells, 4,910,000; white blood cells, 14,100; polymorphonuclears, 90 per cent; small lymphocytes, 10 per cent. The Wassermann reaction was negative. The urine was hazy, with acid; albumin, 1 plus; no sugar and an occasional hyaline cast.

March 23: The patient was up and about and felt well. The gallbladder visualization test was done with the dye administered intravenously. The area of gas in the region of the gallbladder was shaped like a gallbladder, but the organ

13. Moynihan, B.: Brit. M. J. **1**:1, 1928.
14. Rosenow, E. C.: Mayo Clin. **8**:222, 1916.
15. Koch: Ztschr. f. Hyg. u. Infectionskr. **72**:1, 1909.
16. Pesch, K. L., and Hoffmann, V.: München. med. Wchnschr. **75**:1705, 1928.

itself failed to visualize after twelve hours. Dr. J. L. Harvey made the diagnosis of a pathologic gallbladder.

March 24: A surgical consultation was held. Slight icteric conjunctiva, slight tenderness of the abdomen over an enlarged liver, and slight rigidity of the abdominal wall to about the center of the abdomen were noted. Operation was advised.

March 25: The patient was comfortable. The temperature was 99 F., the pulse rate 86 and the respiratory rate 18. The abdominal rigidity was less

Fig. 1.—March 23, 1929: The visualization test was made with dye administered intravenously. The area of gas in the region of the gallbladder was shaped like a gallbladder, but the organ failed to visualize. Note the mottling of gas in the area of the pericystic region.

marked. A tumor mass in the region of the gallbladder could be felt to extend below the margin of the liver. It was tender to light palpation and tympanitic to percussion. A gastro-intestinal series was requested to determine the origin of the air in the gallbladder and to note a communication, if any, with the gastro-intestinal tract.

March 26: A gastro-intestinal series showed persistent deformity of the duodenal cap, which was small, irregular and difficult to visualize. Gas pre-

viously described in the area of the gallbladder on the visualization test had increased in size. It was not connected with the bowel; the fluid level was seen with the patient in an erect posture.

March 27: The patient was transferred to the surgical service. The temperature was 99.8 F., the pulse rate 96 and the respiratory rate 22. The mass was greatly increased in size and was quite tender on palpation and tympanitic on percussion.

Fig. 2.—March 25, 1929: There is a great increase in the gaseous area in the gallbladder region to four times the size shown in figure 2.

Operation.—The operation was performed with the patient under ether anesthesia. The usual gallbladder incision was made, and the peritoneum opened. The colon, omentum, duodenum and stomach were firmly and intimately adherent to the margin of the liver and region of the gallbladder, making a mass the size of a large fist. It was tympanitic; the gas was under considerable tension. The adhesions were separated causing a great amount of bleeding, but the oozing area was packed with hot compresses. The tumor mass was very friable. A number of small abscesses were found in the wall. The outline of the gallbladder was very indistinct. When an attempt was made to find a line of cleavage, the hemorrhage became profuse, but was controlled by hot compresses. It was

deemed expedient merely to drain the gallbladder. A 20 cc. syringe with 19 gage needle was thrust into the tumor; the gas was under sufficient tension to push the plunger out of the barrel of the syringe. Cultures were taken by Dr. Ivan Hall. Coffer-damming strips were used over the entire area. On carrying the strips high up under the surface of the liver, a tear was made in the tumor mass, or a secondary abscess, with escape of rice-soup-like fluid. No odor was noticed. A large tube was introduced into the tip of the tumor. It could not be sutured because of the friability of the tissue. Bleeding was profuse. The finger was introduced into the cavity, supposedly the gallbladder, but no stones were felt. The cavity was filled with thin, bloody fluid, free and clotted blood. No bile was seen. A larger tube was inserted and deep mattress suture succeeded in stopping the bleeding and holding the tube. The tube, the coffer-damming strips of gauze and the protective rubber-dam were brought out through the abdominal incision, which was only partially closed. The patient left the operating table in good condition.

Course.—During the afternoon, the drainage of a thick greenish fluid was profuse; 500 cc. was caught in a syphon bottle. The dressings were saturated and had to be changed several times.

March 28: The temperature was 100 F. and the pulse rate 120. The patient's general condition was good. There was profuse drainage of thick, greenish fluid; the abdomen was not distended and no odor was noticed. No crepitus was felt in the abdominal wall. The patient took fluids freely. He voided voluntarily and passed flatus. Twenty cubic centimeters of Cutter's polyvalent anaerobic serum was given intramuscularly.

March 29: The temperature was 99 F. and the pulse rate 114. No crepitus was noted in the tissues. There was free drainage of bile-stained fluid. Twenty cubic centimeters of polyvalent serum was given intramuscularly.

March 30: The temperature was 99.2 F. and the pulse rate 108. The patient was comfortable and in no pain. There was profuse drainage of clear bile-stained fluid. No crepitus was noted in the tissues. Twenty cubic centimeters of polyvalent serum was given intramuscularly.

March 31: The temperature was 98 F., the pulse rate 94 and the respiratory rate 26. About 8:20 a. m., while on the bedpan straining at the stool, the patient was suddenly seized with severe respiratory distress and became cyanotic. I happened to walk into his room when this occurred. He did not complain of pain, only of the extreme breathlessness. Examination of the lungs gave negative results. Oxygen inhalations gave no relief. At 9:35 a. m., while straining at the stool, he died.

Abstract of the Autopsy Report (Dr. W. C. Johnson).—Autopsy was performed three hours post mortem. The anatomic diagnosis was: suppurative pericholecystitis, cholelithiasis, necrosis with perforation of the neck of the gallbladder, slight biliary cirrhosis of the liver, chronic inflammation and fibrosis of the liver adjacent to the gallbladder, thrombosis of the external and internal iliac veins and pulmonary embolism, the cause of death.

The heart was enlarged. The right ventricle and pulmonary artery opened in situ contained a mass of firm, dark red cylindric and branching thrombi, which extended into the branches of the pulmonary artery.

Examination of the abdomen showed no general peritonitis and no gaseous emphysema. The region of the operative field was well walled off by fibrinous adhesions, forming a pocket into which a rubber sheet drain surrounding a

number of gauze strips extended from a laparotomy wound. A rubber tube drain was sutured into an opening through a layer of tissue which completely covered the region of the gallbladder.

The liver weighed 2,530 Gm. The capsule was thickened, and there was slight biliary cirrhosis. The gallbladder region was covered by a layer of fibrous tissue on the outer surface of which was a fibrinous exudate. A rubber tube drain was sutured in an opening through this tissue near the edge of the liver. An incision through the liver into this region revealed the gallbladder free and collapsed in the apex of a pear-shaped abscess cavity, where it was attached to the cystic duct. Near the neck of the gallbladder was a perforation 1 by 2 cm. through which had been extruded the mulberry-shaped calculus found lying free in the apex of the abscess cavity. The collapsed, slightly thickened, gallbladder wall, roughened on its external surface, contained twelve facetted calculi. The mucosa of the gallbladder appeared practically normal. The wall of the abscess cavity which completely enclosed the gallbladder was made up of fibrous tissue lined with granulation tissue. Several hummocks of granulation tissue projected from the liver into the abscess cavity, causing an irregular contour. On the left side of the gallbladder fossa a layer of fibrous tissue extended for 2 cm. into the liver substance, forming an abscess which communicated with the main pericholecystic abscess cavity.

Microscopic Examination.—The liver showed a slight increase of connective tissue in the portal canals. This tissue was infiltrated with lymphocytes, very marked in some places. The bile ducts appeared normal.

The fossa of the gallbladder was lined by a layer of exudate containing leukocytes, fibrin and masses of yellow pigment. This exudate rested on a layer of granulation tissue, beneath which was a layer of fibrous tissue from which bands of fibrous tissue extended deeply into the adjacent liver tissue.

The gallbladder showed complete loss of nuclear stain. The outline of the layers of the wall could be distinguished. The mucosa and muscularis showed no thickening or infiltration. The outer coat was thickened and studded with masses of granular yellow bile pigment. Sections stained for bacteria showed very few long filamentous, gram-negative organisms in the outer coat.

Abstract of the Bacteriologic Report (Ivan Hall, Ph.D.).—Two specimens were taken from the field of operation.

The specimen from the blood around the tumor mass, after the surrounding adhesions were separated, showed a pure culture of an atypical *Bacillus welchii.*[12] The specimen from the cavity proper also showed atypical *Bacillus welchii* in pure culture. Ten cubic centimeters of blood from the median basilic vein three hours after operation was negative on culture.

Bacteriologic culture studies at autopsy revealed the heart blood to be normal and the bile showed gram-positive filaments and rods resembling those isolated at the time of operation. Three varieties of staphylococcus were isolated: *Micrococcus aureus, Micrococcus aurantiacus, Micrococcus epidermis* and *Bacillus tertius.*

The Cutter's triple anaerobic serum contains in each cubic centimeter 5,000 guinea-pig minimum lethal doses of *Bacillus oedematiens* (*Bacillus novyi*) toxin; 300 rabbit minimum lethal doses of *Bacillus welchii.*

This serum is similar to that developed by Weinberg[17] and used by the French in cases of gas gangrene during the World War.

17. Henry, Herbert; and Lacey, Margaret: J. Path. & Bact. **23**:283, 1920.

COMMENT

There was cholecystitis with cholelithiasis of considerable duration. The patient's first attack of biliary colic three weeks before admission to the hospital may have inaugurated the incarceration of the mulberry calculus which was found at autopsy ulcerated through the wall at the neck of the gallbladder.

The walls of the gallbladder on microscopic study disclosed pathologic changes extending from the necrotic mucosa to the thickened pericholecystic fibrous tissue. The gallbladder was entirely separated from the liver and the enveloping bridge of fibrous tissue.

The infection was of longest duration and of greatest intensity in that portion of the pericholecystic cavity corresponding to the sulcus for the gallbladder. This is evidenced by the microscopic slides and the small abscess deep in the liver margin of the sulcus.

It is improbable that the infection was hematogenous, since the blood cultures both ante and post mortem were negative; further, there was no gaseous emphysema elsewhere before or after death. Consideration must be given to the effect of the triple anaerobic serum which may have controlled whatever blood infection may have been present.

Ascending or descending infection via the bile to the gallbladder seems improbable, because the mulberry calculus blocked the cystic duct until it ulcerated through the neck of the gallbladder. When this occurred cannot be conjectured. This necrotic area furnished a favorable nidus for localization and growth of the gas bacillus. Intracholecystic accumulation of gas may have been a factor in the extrusion of the calculus. The abscess cavity must have been developed before the extrusion.

Extension from the gallbladder is a possibility, but the microscopic studies are not suggestive.

Most likely the gas bacillus was an auto-infection extending directly from the liver or indirectly from the liver to the perivesicular tissue, the primary extension being across the bridge of adhesions between the bowels, stomach, duodenum and colon and the under surface of the liver. As the gallbladder was completely enveloped up to the cystic duct by a preformed, well developed fibrous tissue, adhesions were prevented from forming between the gallbladder and other viscera, excluding direct extension to the gallbladder.

The intramuscular injection of the triple anaerobic serum (Cutter) seems to have had a favorable influence in controlling the gas bacillus infection.

The postoperative course was remarkably smooth, with no extension of the gaseous emphysema until the pulmonary embolus developed, causing death on the fourth postoperative day.

PRIMARY, ISOLATED LYMPHOGRANULOMATOSIS OF THE STOMACH *

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Ever since the time of Billroth, Hodgkin's disease, by general agreement, has been excluded from the category of surgical diseases. The reason for considering the disease as nonsurgical was due not so much to the technical difficulties entailed as to the unfavorable end-results. The fact that pathologists subsequently demonstrated that the disease might begin as an isolated lesion did not alter the surgical status of the disease. Apprisal of the occurrence of isolated lesions failed to modify previous opinion, because the organs described as the seats of primary involvement, such as the spleen, the liver, the bone-marrow and the lungs, either did not lend themselves to surgical extirpation or did not lead to clinical manifestations that might have permitted early recognition. In the past few years, a number of patients with isolated lymphogranulomatosis of the gastro-intestinal tract have been treated by radical resection, generally under a mistaken clinical diagnosis. The results obtained in these cases are sufficiently favorable to challenge the prevailing noli-me-tangere policy and to call for a reconsideration of the question. Of particular interest, especially in connection with the case here reported, are the isolated lesions of the stomach, the phase of the subject with which this paper will mainly deal. For a summary of the primary and limited intestinal cases, the reader is referred to Goedel [1] Slovacek,[2] Pissarewa [3] and the splendid article of Coronini.[4]

The first case of strictly isolated lymphogranulomatosis of the stomach was reported by Steindl,[5] in 1924. The preoperative diagnosis was gastric carcinoma. At operation an infiltrating tumor, involving

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1. Goedel, A.: Zur Kenntnis des primären, isolierten Darmlymphogranuloms, Wien. klin. Wchnschr. **42**:426 (April 4) 1929.

2. Slovacek, O.: Prispevek k lymfogranulomatose zezivaciho traktu, Časop. lék. česk. **68**:503 (April 5) 1929.

3. Pissarewa, T.: Lymphogranulomatosis (Paltauf-Sternberg) des Verdauungstraktes, Arch. f. klin. Chir. **149**:75 (Dec.) 1927.

4. Coronini, C.: Ueber das Paltauf-Sternberg'sche Lymphogranulom, Beitr. z. path. Anat. u. z. allg. Path. **80**:405, 1928.

5. Steindl, H.: Ueber einen Fall von Lymphogranulomatose des Magens, Arch. f. klin. Chir. **130**:110 (April) 1924.

the pyloric and prepyloric regions, was found, together with a number of glands the size of a hazelnut in the adjacent lesser omentum and in the gastrocolic ligament. Exploration of the remainder of the abdominal organs failed to disclose other lesions. A resection was performed, and the patient made an uneventful recovery. Postoperative observation over a period of a year yielded no evidence of recurrence or development of other foci. Later in the same year, Neuber [6] presented before the Eleventh Hungarian Surgical Congress a case of isolated Hodgkin's disease that was clinically diagnosed as ulcer. Partial gastric resection led to the discovery that the lesion was lymphogranulomatous. In 1926, a case similar to that of Steindl was observed in South Manchuria by Kan.[7] A woman, aged 52, was operated on for a suspected carcinoma, and a gastric tumor and three glands the size of a pea were resected. The growth, when examined microscopically, proved to be Hodgkin's granuloma. The postoperative course was uneventful for a month, when persistent vomiting set in and led to death. Autopsy disclosed an obstruction at the site of the anastomosis and, in addition, lesions that were diagnosed as those of an old case of tuberculosis of the apical and cervical glands. No other morbid processes were noted grossly.

In May, 1926, von Redwitz [8] presented a case before the Surgical Society of Munich, in which the preoperative diagnosis was peptic ulcer. The pyloric lesion encountered at operation led to a suspicion of carcinoma and occasioned a resection. The histologic diagnosis of the surgical specimen was lymphogranulomatosis. The following year (1927) a detailed report was published by Thiemer [9] dealing with a case of isolated gastro-intestinal lymphogranulomatosis observed at the clinic of von Redwitz. Presumably, the reports of both authors refer to the same case. The histologic appearance of Hodgkin's disease in the case of Redwitz and Thiemer was complicated by the presence of numerous foreign bodies and foreign-body giant cells. Further difficulty in the elucidation of the origin of the disease resulted from the circumstance that a month prior to admission the patient had drunk hydrochloric acid. Following recovery from the operation, the patient left the hospital and did not return for observation. In 1927,

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6. Neuber, E.: Magengranulomatose, Zentralorg. f. d. ges. Chir. u. ihre Grenzgeb. **31**:309, 1925.

7. Kan, J. N.: Report on a Case of Lymphogranuloma in the Stomach, J. Orient. Med. **5**:9 (July) 1926.

8. von Redwitz, E.: Vereinigung Münchener Chirurgen, Zentralbl. f. Chir. **53**:2087 (Aug. 14) 1926.

9. Thiemer, P. H.: Zur Kasuistik der isolierten Lymphogranulomatose des Magendarmtraktes, Deutsche Ztschr. f. Chir. **205**:404 (Sept.) 1927.

Froboese [10] described a case in a woman, aged 63, in whom a prepyloric tumor and slightly enlarged lesser omental glands were resected for supposed carcinoma. The microscopic diagnosis was Hodgkin's granuloma. Following convalescence, further search for evidence of other lymphogranulomatous foci yielded negative results.

An interesting case observed by Vasiliu [11] in 1926 and reported in 1929 was that of a medical student who was thought to be suffering from a gastric ulcer. Failure of response to medical treatment led to a partial resection of the stomach and extirpation of the glands along the lesser curvature, one of which was the size of a walnut. After recovering from the operation, the patient was able to finish her medical course without physical handicap, and she was still well when Vasiliu's manuscript was submitted for publication. Other cases, such as those of Gossman and of Lubarsch,[12] which are referred to at times as isolated gastric Hodgkin's disease, but in which limitation to the stomach is questionable, are best omitted from the category of strictly isolated cases.

There are a number of cases reported, besides those cited, in which the lymphogranulomatosis was localized to the gastric region but not strictly limited to the stomach and the perigastric lymph glands. The case described by Scott and Forman [13] can be designated as regional in that the disease, although not limited to the stomach, had not spread beyond the contiguous structures. According to these authors, the lymphogranulomatosis led to a shrinking and a thickening that extended from the pylorus to from 3 to 5 cm. beyond the cardia into the esophagus. The wall of the stomach was adherent to the upper pole of the spleen and to the diaphragm. The perigastric and peripancreatic glands were enlarged. There was no further evidence of overgrowth elsewhere, either in the lymph nodes or in the mucous membranes. Hayden and Apfelbach [14] reported three cases of gastro-intestinal lymphogranulomatosis, in one of which the disease was localized to the stomach and its vicinity. In a second case there was an associated involvement of

10. Froboese, C.: Bermerkungen an der Hand eines Falles von Lymphogranulom des Magens, Beitr. z. path. Anat. u. z. allg. Path. **77**:363 (April) 1927.

11. Vasiliu, T.: L'ulcère lymphogranulomateux gastroduodenal, Sang **3**:257 1929.

12. Lubarsch, quoted by Konjetzny, G. E.: Die Entzündung des Magens: Lymphogranulomatose, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1928, vol. 4, part 2, p. 1060.

13. Scott, E., and Forman, J.: Lymphoblastomata of the Gastrointestinal Tract: With a Report of a Case of Hodgkin's Disease of the Stomach, Ohio State M. J. **12**:323 (May) 1916.

14. Hayden, H. C., and Apfelbach, C. W.: Gastro-Intestinal Lymphogranulomatosis, Arch. Path. **4**:743 (Nov.) 1927.

the lower mediastinal lymph glands. In the case reported by Sussig,[15] in a man, aged 42, the primary lesions was located in the pars media on the lesser curvature of the stomach and adherent to the pancreas and the liver. The mesocolon and the root of the mesentery were infiltrated, and the perigastric, periaortic and peripancreatic lymph glands were enlarged. The reason for separating the regional from the strictly isolated cases is that the former are too extensive for surgical extirpation.

A great deal of circumspection is necessary before a case of gastrointestinal lymphogranulomatosis can be considered as strictly isolated. Gross lesions may be present in organs inaccessible to the surgeon who performs the operation and, therefore, they may be entirely overlooked. Pissarewa [3] mentioned a case observed by Pokotilo and Busni, in which a lymphogranulomatous cecum was the only lesion discovered at operation. Postmortem examination disclosed a solitary granulomatous node in the spleen. In case 2 reported by Vasiliu,[11] in which a gastric resection for Hodgkin's granuloma had been performed eight hours antemortem, the autopsy likewise revealed a small nodule in the spleen. Even an autopsy does not insure the discovery of lesions outside of the digestive tract unless a microscopic search is instituted. In a case of diffuse lymphogranulomatosis of the intestinal tract with perforation of the jejunum, recorded by Warfield and Kristjansen,[16] the splenic and hepatic involvement was a microscopic revelation. The generalized nature of the process in the case of Bianchi,[17] in which the principal gross changes were localized in the stomach, was detected by histologic means. Under exceptional circumstances, even the most painstaking gross and microscopic examination may be insufficient to discover the primary source, as in the case described by Sternberg.[18] This author cited an instance of gastric lymphogranulomatosis in a person who, six years prior to death, was treated by roentgen rays for a large mediastinal tumor. No remnant of the growth which, according to Sternberg, indubitably represented granulomatous glands could be identified at autopsy.

The case here reported is unique in the literature on lymphogranulomatosis of the stomach in that it is the only one, so far as could be ascertained, in which a careful clinical history and a gross and microscopic study of the tissues obtained at necropsy showed that the disease was limited to the stomach and the perigastric lymph glands. The other

15. Sussig, L.: Sul linfogranuloma maligno dello stomaco, Pathologica **21**:397 (Aug. 15) 1929.

16. Warfield, L., and Kristjansen, H. T.: Hodgkin's Disease of the Intestines; with Report of a Case, Bull. Johns Hopkins Hosp. **27**:24 (Jan.) 1916.

17. Bianchi, A. E.: Granulomatosis, Semana méd. **1**:432 (March 16) 1922.

18. Sternberg, C.: Die Lymphogranulomatose, Klin. Wchnschr. **4**:529 (March 19) 1925.

cases of isolated Hodgkin's disease referred to were, with the exception of Kan's,[7] surgical cases in which operation was followed by recovery, and examination of other tissues was therefore precluded. In Kan's case an autopsy was performed, but a complete microscopic study was not made post mortem, at least so far as can be determined from the rather complete summary of the case in English.

CASE REPORT

M. G., a white man, aged 62, who first entered the Cook County Hospital on June 30, 1928, stated that in October, 1926, he began to notice a burning pain in the left hypochondrium; it appeared regularly at 4 p. m. and lasted until the evening meal. On account of this distress cholecystectomy and appendectomy were performed in May, 1927. Subsequent to the operation, the pain appeared following each meal, usually after an interval of from one-half to four hours. Eructations of acid were particularly prominent in the afternoon. The ingestion of soda was tried a number of times, but it failed to afford relief. The effect of food on the pain had not been tested. At the age of 28 the patient had suffered from postprandial, epigastric burning of one month's duration. Tablets prescribed by a physician appeared to check the attack. The patient remained well for five years; then he suffered from an excruciating knifelike pain in the epigastrium, which required morphine for relief. A similar attack occurred five years later, at the age of 38. In 1912, a brief siege of "water-brash" of two months' duration, unassociated with pain, was experienced. From that time until October, 1926, the patient had no complaints. Aside from loss of appetite of six months' duration and a loss of 30 pounds (13.6 Kg.) during the eighteen months of illness, a general inventory of symptoms afforded no significant information.

The temperature and the pulse and respiratory rates were normal. The blood pressure was 138 systolic and 72 diastolic. Except for the presence of a scar on the right upper guadrant, abdominal examination gave negative results. Examination of the blood revealed: hemoglobin, 60 per cent; erythrocytes, 3,330,000; white blood cells, 7,600, of which 76 per cent were neutrophilic leukocytes, 20 per cent lymphocytes and 4 per cent monocytes. The Ewald meal yielded 60 cc. with 45 per cent free and 18 per cent combined acidity. Of four stools passed on successive days, the first two gave a positive and the second two a negative test for occult blood. The Wassermann reaction of the blood was negative. A roentgenogram of the stomach (fig. 1) demonstrated a constant shallow irregularity on the lesser curvature in the prepyloric area, opposite which was an incisura. Projecting from the proximal margin of the incisura was a persistent niche. The roentgen diagnosis was indeterminate.

The patient improved steadily on Sippy management, but the response was neither as rapid nor as complete as is usual in cases of uncomplicated ulcer. The patient left the hospital on July 30, 1928, with instructions to report to the gastrointestinal follow-up clinic. At his first visit to the clinic on August 2, he weighed 144 pounds (65.3 Kg.). He was placed under ambulatory management for ulcer and was permitted to return to his occupation. He gained weight and strength and, except for slight pain that could be controlled by returning to a strict regimen, he felt well. He visited the clinic last on July 18, 1929, when he weighed 161 pounds (73 Kg.) and stated that he was having no pain.

The patient reentered the hospital on March 18, 1930, asserting that following discharge in July, 1928, he remained relatively symptom-free for three months.

After that time the previous burning pain returned at irregular intervals, but it was merely diurnal and remained amenable to treatment. Three months prior to his second admission, in December, 1929, he began to suffer from pain at night, and six weeks later the epigastric burning became almost continuous. The alkaline powders, according to the patient, served as "kindling for the internal fire" during the latter stage. Vomiting after the ingestion of food, which previously occurred occasionally, now appeared almost daily. Emesis afforded only partial relief. Within the last few weeks complete anorexia had appeared. The loss of weight

Fig. 1.—Roentgenologic appearance of the stomach on July 24, 1928. The prepyloric deformity was constant fluoroscopically and in a series of films.

during the two months preceding admission was estimated as 10 pounds (4.5 Kg.). The accompanying weakness was profound.

Physically, the patient was fairly well nourished and did not appear anemic. Abdominal examination disclosed, in addition to the previous operative scar, a midepigastric mass which was freely movable and devoid of tenderness. No other noteworthy abnormalities were recorded. Aspiration after an Ewald test meal yielded 120 cc. of gastric contents with 18 per cent free and 30 per cent combined acidity. The chemical test for occult blood was positive both for the contents of the stomach and for those of the stools. Roentgen examination of the stomach

with barium sulphate (fig. 2) demonstrated a constant annular deformity of irregular density and contour involving the pars pylorica and the distal portion of the pars media. This lesion occasioned retention of 50 per cent of the six hour meal. The roentgen diagnosis was carcinoma. The Wassermann reaction was negative.

The patient was transferred to the surgical service with a preoperative diagnosis of gastric carcinoma superimposed on a peptic ulcer. Laparotomy, performed on April 4, 1930, disclosed a semielastic tumor involving the distal third of the

Fig. 2.—Roentgenogram of the stomach taken on March 27, 1930, demonstrating the annular constricting deformity involving the pars pylorica and the distal portion of the pars media.

stomach, with a number of enlarged perigastric glands as large as hazelnuts. The surgeon decided to delay radical resection until the general condition of the patient could be improved through relief of the obstruction. He therefore performed a posterior gastro-enterostomy. Convalescence was uneventful until the morning of April 23, nineteen days after operation, when the patient complained of epigastric pain. Shortly before midnight, emesis occurred, and this was repeated several times on the following day. Acute gastric dilatation was suspected, and lavage

was instituted. On the morning of April 25, the patient complained of abdominal pain, but he was not believed to be in a serious condition. In the afternoon, following copious emesis of a greenish fluid, the patient rapidly weakened and died.

Autopsy.—The postmortem examination was made by Dr. R. H. Jaffé, who pointed out the following pertinent conditions: Although the abdomen was somewhat scaphoid, the stomach, duodenum and proximal jejunum were enormously dilated. The lack of abdominal distention was due to the fact that the gastric dilatation involved merely the proximal two-thirds, which buried itself subcostally and forced the diaphragm upward. The distal one third of the stomach lacked distensibility on account of the presence of a rigid infiltrating tumor. Eleven centimeters from the duodenojejunal junction, the intestine was twisted at an angle of 90 degrees, and it was surgically anastomosed to the stomach. Through the loop formed by that portion of jejunum that was fixed by the ligament of Treitz on the one hand and the point of anastomosis on the other, herniation of the remainder of the jejunum and all but the terminal ileum had occurred. The herniated loops were readily reduced, and normal conditions were thereby restored. Death was assigned directly to the high-lying obstruction caused by the internal incarceration.

Except with regard to the stomach and perigastric lymph glands to be described in detail, the postmortem observations require no elaboration for purposes of this paper. A painstaking search disclosed no gross evidence of lymphogranulomatosis other than in the stomach, the beginning duodenum and the perigastric lymph glands. The essential changes noted at necropsy are epitomized in Dr. Jaffé's anatomic diagnosis, which was: Hodgkin's lymphogranuloma of the distal portion of the stomach, the beginning duodenum and the perigastric lymph glands; recent gastrojejunostomy; herniation and incarceration of the small intestines through the anastomotic loop; high intestinal obstruction; recent fibrinous peritonitis; chronic focal bronchopneumonia of the left lower pulmonary lobe; inflammatory softening of the spleen; cloudy swelling of the liver, the kidneys and the myocardium; generalized emaciation; brown atrophy of the myocardium; endocardial sclerosis, and fibrous obliteration of both of the pleural cavities.

Gross Description of the Lymphogranulomatous Lesions.—The stomach was greatly enlarged, owing to a marked dilatation of the proximal two-thirds. The distal one-third, which was free from distention, was the seat of a soft, somewhat elastic infiltration which began 7.5 and 23 cm. proximal to the pyloric ring on the lesser and greater curvatures, respectively, and terminated 2.2 cm. distal to the pyloroduodenal junction. There was no gross extension of the tumor beyond the gastric or duodenal walls.

On opening the stomach (fig. 3), the dilated portion was seen to be finely mammillated, devoid of rugous folds and intact. The wall was thinned in proportion to the degree of distention of the organ. A recent, functioning gastro-enterostomy stoma was present on the posterior wall proximal to the infiltration. A tumor occupied the distal one third of the stomach, and had produced a marked thickening of the gastric wall without leading to stenosis of the lumen. The circumference of the pyloric ring, as measured on the inside of the stomach, was 4 cm. The gastric circumference was 7.5 cm. at a point 2 cm. proximal to the ring. The lining of the infiltrated portion of the stomach was grayish white and extensively ulcerated. The ulcerations were, for the most part, superficial and irregular in outline, and they possessed sloping edges. Nowhere did the base of an ulcer extend below the niveau of the normal mucosa. The borders of the infiltrate were slightly raised and could be clearly defined, the proximal one being roughly scalloped and the distal one only slightly wavy in outline.

The cross-section of the wall of the stomach in the involved area (fig. 4) exhibited a striking increase in thickness, which reached its maximum at a point 5 cm. proximal to the pylorus where it measured 2.5 cm. In passing both caudad and craniad from the point of maximum thickness, there was a gradual tapering down until the limits of the tumor were reached. The increase in thickness was due to grayish-white, homogeneous, adenoid-like tissue, succulent and semifirm in consistency. The identification of the individual layers was obscured except at

Fig. 3.—The interior part of the stomach. The greater portion of the anterior wall has been removed. The gastro-enterostomy stoma is situated proximal to the upper margin of the granulomatous infiltrate.

the extremities of the growth where the gray muscularis could be seen subjacent to the white foreign tissue.

A number of the lymph glands in the gastrohepatic omentum, located in the prepyloric area, were increased in size, the largest measuring 3 cm. in diameter. The tissue comprising these glands was identical with that noted in the stomach. A few prepyloric glands similar to but smaller than those in the lesser omentum were found in the gastrocolic ligament. The peripancreatic and periaortic glands were not enlarged.

Microscopic Description.—Sections from various portions of the stomach and from the pyloroduodenal junction showed essentially the same changes and therefore lend themselves to a composite description. Figures 5 and 6 furnish representative pictures of the histopathologic condition found. Since the morphologic details differed in no way from the microscopic appearance of Hodgkin's disease found elsewhere, the finer minutiae can be omitted.

The mucosal layer was almost completely replaced by a granulation tissue consisting of short, spindle-shaped fibroblasts and thin-walled capillaries, in which the following types of cells were embedded: round cells of a lymphocytic character mainly small; larger cells with barely discernible cytoplasm containing large, oval and round, pale, vesicular nuclei; eosinophils and plasma cells of the usual type; distinctive giant cells with large, round, irregular or lobulated nuclei that were rich in chromatin with distinctly oxyphilous nucleoli. At times these giant cells

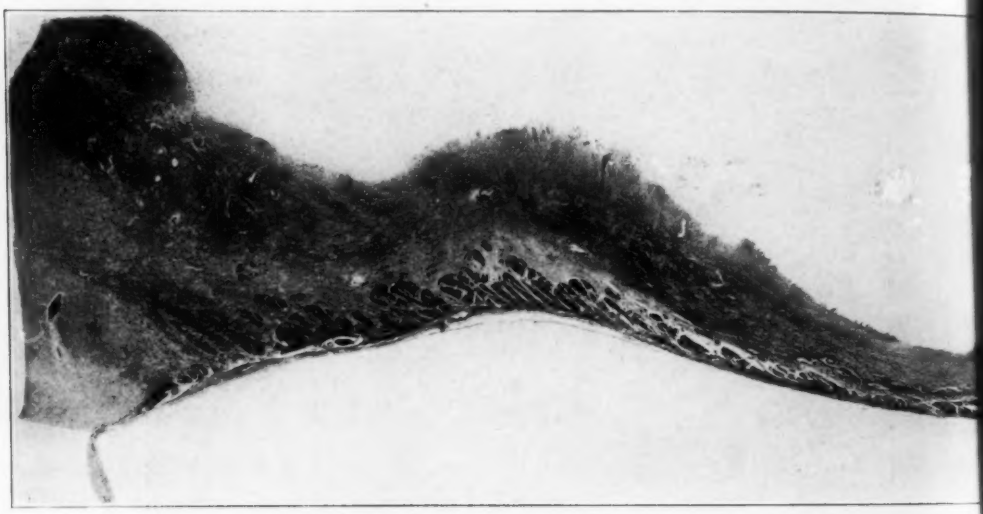

Fig. 4.—Cross-section of the gastric wall taken from the region proximal to the area of maximum thickness.

(Sternberg-Reed) appeared multinucleated. The round cells and histiocytes predominated. Eosinophils were prominent, whereas plasma cells were encountered relatively infrequently. The Sternberg-Reed giant cells were numerous, as many as 15 being found in a single, high power field. Only a few widely separated, but well preserved, glandular elements remained to indicate the site of the original tunica propria. The muscularis mucosa was almost completely destroyed.

The prodigious thickening of the involved area was due mainly to the increase of the submucous layer, which in places constituted as much as nine tenths of the gastric wall. Throughout the involved portion the infiltration in the submucosa passed imperceptibly into the overlying mucosa. Where the involvement was minimal, the cellular accumulations of the submucosa were separated from the muscularis by a condensation of collagen fibers only slightly infiltrated by cellular elements. In approaching the areas of maximum involvement, this fibrous septum became more and more obscured by extensions of dense cellular infiltrates which obliterated the zone of division between the submucous and muscular layers. In

a number of areas, the polymorphocellular character of the infiltrate was striking, whereas in other areas consisting mainly of histiocytes the appearance was relatively uniform. The invading and proliferated cells comprising the submucosa were identical with those found in the mucosa.

The muscular layer appeared fairly normal in the areas of least involvement. As the region of maximum infiltration of the gastric wall was approached, extensions from a fibrous layer in the floor of the submucosa insinuated themselves between the bundles of muscle. Progressing still further, one found numerous cells embedded in, and augmenting, the invading fibrous septums. The muscular

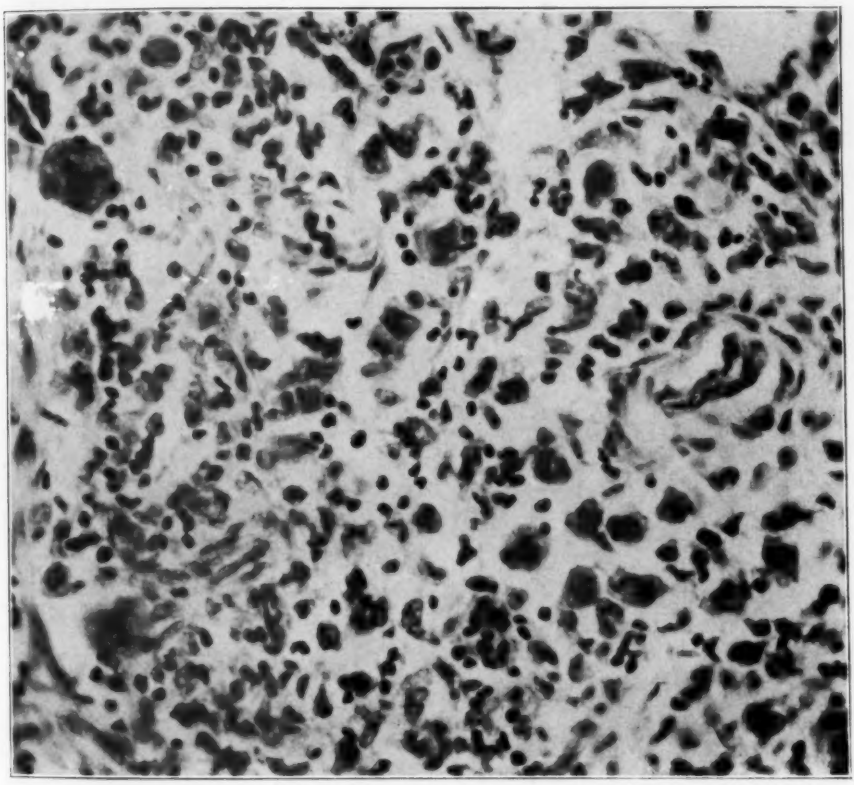

Fig. 5.—Photomicrograph of the mucosa, illustrating the polymorphocellular character of the granuloma; × 400.

layer, still retaining its identity, was notably increased in thickness as a result of this fibrocellular incursion. Gradually the cellular elements became more and more numerous and the elements of the muscle and the connective tissue less and less conspicuous, until they were completely obscured. The individual cells comprising the infiltrates did not differ from those present in the overlying layers.

A slight increase of the serous coat, due mainly to fibroblasts and edema fluid, was noted in the portions with minimal thickening. Passing toward the area of greatest involvement, one found that the layer became invaded by an increasing number of cellular elements until the point was reached where the thickened

serosa coalesced with the muscularis. Here, identification of individual layers was impossible, and the entire gastric wall assumed a uniform appearance. The infiltrated cells of the serosa were mainly of the round type, associated principally with plasma cells and histiocytes. Sternberg-Reed giant cells were infrequent in this layer.

The histologic appearance of the lymph nodes located in the region of the tumor was practically identical with that of the gastric wall in the region of

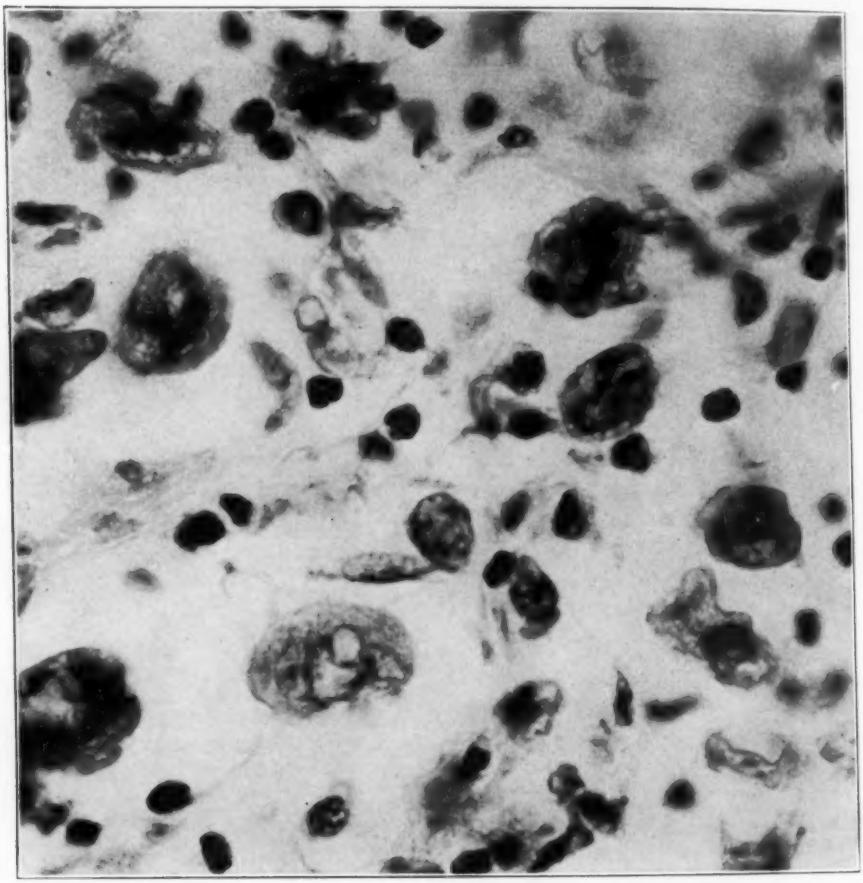

Fig. 6.—A field from the mucosa exhibiting the pleomorphism and finer morphologic structure of the Sternberg-Reed giant cells; × 1,100.

maximum involvement. The characteristic polymorphocellular granulomatous tissue, with an abundance of monolobulated and multilobulated giant cells, was well exhibited. Changes suggestive of Hodgkin's disease were not noted in other sections.

COMMENT

That Hodgkin's disease may begin primarily, not only in lymph glands, but also in the adenoid structures of various organs is firmly

established. Acknowledging a primary origin in the gastro-intestinal tract, it would seem, theoretically, that surgical extirpation would be the treatment of choice in localized cases. The fact that lymphogranulomatosis, although probably inflammatory, behaves clinically like a malignant growth does not militate against the justification or the desirability of radical removal. As Pissarewa contended, no one would refrain from operation in the case of an operable carcinoma merely on account of a possible recurrence and unfavorable outcome. Nor would one allow a localized tuberculous focus to remain untouched in the gastro-intestinal tract because it is inflammatory. In the absence of any other known effective and reliable therapeutic agent, the inherent character of the disease, the tendency to recurrence and the fatal outcome do not constitute valid objections to surgical removal. Particularly is this true with regard to isolated lesions of the stomach when early recognition is feasible, the involved organ is accessible and the operative danger is relatively slight. Naturally, discretion must be exercised in selecting the cases for operation since a radical operation in a case of more or less disseminated lymphogranulomatosis is as futile as in a patient with diffuse carcinomatosis or sarcomatosis. It is, of course, necessary to keep in mind that the presence of small lesions outside of the digestive tract that do not permit clinical demonstration or identification cannot be eliminated and that, therefore, a guarded prognosis should be made in all cases.

These theoretical considerations receive support from practical experiences with isolated lymphogranulomatosis of the gastro-intestinal tract. With regard to the stomach, the cases of Steindl,[5] Froboese[10] and Vasiliu[11] are particularly noteworthy. Steindl's patient was free from evidence of recurrence when last observed a year after resection. Until the time of publication of Froboese's report, which was five months after operation, the patient had not returned for medical aid, and she was assumed to be in good health. The most striking surgical result was obtained in the case of the medical student reported by Vasiliu. The patient, following a gastric resection in 1926, completed her medical course and was entirely well when last observed, in 1929. It is likely that within the series of the resected cases of lymphoblastoma with favorable outcome reported by Holmes, Dresser and Camp,[19] one or more instances of Hodgkin's disease are included. Should recurrences or independent foci subsequently appear, their presence will hardly detract from the value of the treatment which has been instituted. A few years of relief from symptoms justifies a radical procedure, as illustrated in the following case of intestinal

19. Holmes, G. W.; Dresser, R., and Camp, J. D.: Lymphoblastoma: Its Gastric Manifestations, with Special Reference to the Roentgen Findings, Radiology **7**:44 (July) 1926.

lymphogranulomatosis. Biebl [20] recorded that a man, aged 25, who complained of symptoms referable to the lower part of the abdomen, underwent resection of the small intestine and the attached portion of the urinary bladder on June 12, 1920. The microscopic diagnosis was lymphogranulomatosis. The patient remained well for five years when symptoms referable to the upper part of the abdomen appeared. These had been present six months when, on Dec. 31, 1925, the patient was operated on for a perforative peritonitis and 40 cm. of lymphogranulomatous jejunum was resected. White nodes and infiltrates were in the omentum and the mesentery. The patient again made an uneventful recovery and returned to his occupation as a farmer.

Since available evidence indicates that surgical measures are of value in the treatment for isolated gastric lymphogranulomatosis, it follows that the diagnostic aspects of the disease merit consideration. In no case of primary, isolated, gastric Hodgkin's disease has the diagnosis been made prior to the operation or autopsy. This statement is not surprising in view of the fact that clinically there is no local feature of the disease that, in the present state of knowledge, is distinctive. Carcinoma or ulcer is generally diagnosed, particularly the former. Characteristic systemic manifestations are, as a rule, lacking in the localized stage. Paroxysms of fever (Pel-Epstein), which are highly suggestive of Hodgkin's disease, are generally absent until the disease becomes more or less disseminated. Sussig's [15] patient, in whom the disease was not actually isolated, but rather localized to the region of the stomach, suffered from an intermittent type of high temperature which reached 41 C. (105.8 F.). In all three cases of lymphogranulomatosis with gastro-intestinal involvement observed by Sussig, he noted the association of an intermittent fever, a brownish-red discoloration of the skin and excessive desquamation of the epidermis involving especially the soles and the palms. Other authors have not observed this syndrome, and therefore no diagnostic importance can be attached to it. The hematologic features of eosinophilia and monocytosis are, like fever, usually absent in cases with isolated lesions. In the case of Bianchi,[17] in which the diagnosis of Hodgkin's disease was made on hematologic and clinical evidence, the gastric lesion formed only part of a generalized involvement.

Although isolated gastric lymphogranulomatosis cannot be diagnosed by current clinical methods, the lesion usually leads to surgical exploration when its presence can at least be suspected. Steindl [5] noted in his case that the pyloric tumor was flat, infiltrating, soft and resilient, and was accompanied by many isolated glands as large as a hazelnut. From the gross characteristics of the gastric tumor and the adjacent nodes,

20. Biebl, M.: Beitrag zur intestinalen Lymphogranulomatose, Deutsche Ztschr. f. Chir. **198**:104 (Aug.) 1926.

he suspected the presence of a lymphosarcoma or tuberculosis. In Kaznelson's [21] description of operative observations, he mentioned a circular infiltration of the pylorus which gave the impression of a benign stenosis rather than of a malignant condition. The mesenteric lymph glands were recorded to be from the size of a hazelnut to that of a walnut. In the case here reported, the gastric infiltration resembled that found in syphilis of the stomach, but the number and character of the glands were not in accord with a diagnosis of gastric syphilis. From a consideration of the facts available, the disclosure at operation of a soft, flat, infiltrating tumor limited to the distal portion of the stomach, associated with many isolated, relatively large, soft, cream-colored, succulent glands, should arouse the suspicion of a gastric lymphogranulomatosis. There is another type of lymphogranulomatous infiltration in which the gastric folds bear a close resemblance to cerebral convolutions as described by Sternberg.[18] This form tends to involve the stomach diffusely and can readily be confounded with gastric aleukemic lymphadenosis.

For a final diagnosis the use of the microscope is indispensable. Even after histologic sections are available, the interpretation is not always a simple matter especially in the early stages, as exemplified in the initial biopsy of the generalized case reported by Hayden and Apfelbach.[14] The main difficulty lies in distinguishing between lymphosarcoma and lymphogranulomatosis. In the case of Hodgkin's disease reported by Terplan and Wallesch [22] the microscopic changes in blocks from certain parts of the gastro-intestinal tract did not permit differentiation from a lymphoblastic sarcoma. Differentiation between lymphosarcoma and Hodgkin's disease could not be made from the histologic appearance of the primary tumor in the case described by Pamperl and Terplan.[23] In the adjacent mesenteric lymph glands, however, the morphologic appearance was characteristic of lymphogranulomatosis. Another possibility of error in bioptic diagnosis, which is remote, however, was mentioned by Konjetzny.[12] This author recorded a case of colloid carcinoma of the pylorus with carcinomatous glands in the adjacent area and lymphatic nodes as large as walnuts extending along the lesser curvature and reaching to the cardia. The latter glands, which at the operation were assumed to be carcinomatous, proved microscopically to be lymphogranulomatous.

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21. Kaznelson, P.: Ueber einen Fall von Nischenbildung und Pylorusstenose infolge Lymphogranulomatose des Magens, Wien. Arch. f. inn. Med. **7**:117, 1923.

22. Terplan, K., and Wallesch, E.: Ein Fall von intestinaler Lymphogranulomatose, Med. Klin. **19**:1428 (Oct. 28) 1923.

23. Pamperl, R., and Terplan, C.: Ein Beitrag zur intestinalen Lymphogranulomatose, Med. Klin. **21**:1679 (Nov. 6) 1925.

The effect of irradiation on lymphogranulomatous tissue, especially in the hyperplastic stage, renders the roentgen rays of some diagnostic, as well as therapeutic, value. When surgical intervention is contraindicated, a response to roentgen treatment would place the case in the group of so-called malignant lymphomas. Holmes, Dresser and Camp [19] recorded a case in a woman, aged 64, who had been receiving treatment with roentgen rays for enlarged peripheral lymph nodes, which were proved by biopsy to be lymphoblastomatous. The development of gastric symptoms led to an examination with a barium meal. An irregular filling defect devoid of peristalsis was found involving the lower third of the stomach. After roentgen irradiation the gastric symptoms improved, and the filling defect diminished in extent; it became difficult of demonstration and no longer interfered with the passage of peristaltic waves. Little need be said regarding the therapeutic value of the roentgen rays in inoperable gastric lymphogranulomatosis. If nothing more, at least a great deal of suffering can be spared the patient by the judicious use of the roentgen rays. In any case in which the possibility of a lymphogranulomatous process may be entertained, the surgeon should remove a gland for biopsy. If carcinoma is discovered, nothing is lost. If, on the other hand, the tumor proves to be Hodgkin's disease, the patient's suffering may be ameliorated and his life prolonged by roentgen therapy.

SUMMARY

Pathologists have known for many years that lymphogranulomatosis may have its origin, not only in lymph glands, but in any organ or structure that normally contains adenoid tissue. The fact that primary growths were known to occur in the spleen, the liver, the bone-marrow and the lung attracted little surgical attention on account of the inherent difficulties that lay in the way of early diagnosis and of surgical extirpation. With regard to primary diseases of the gastro-intestinal tract, and particularly of the stomach, prompt manifestations are the rule; diagnosis of the presence of a lesion is not difficult, and surgical removal is relatively safe.

Six cases of primary, isolated Hodgkin's disease of the stomach are recorded in the literature. The preoperative diagnosis was either carcinoma or ulcer, and gastric resection was performed in all of them. Five patients recovered and remained well for as long as they were observed. A sixth patient died, a month after operation, from obstruction at the stoma. No gross evidence of other lymphogranulomatous lesions was found post mortem, but no mention of microscopic examination of the various organs was made. The seventh case of isolated Hodgkin's disease of the stomach, the first to be reported in this country, is unique in that a complete history and a painstaking gross

and microscopic examination at necropsy failed to disclose any previous or associated lesion elsewhere in the body.[24]

The clinical diagnosis of isolated lymphogranulomatosis of the stomach is hardly possible in the present state of knowledge. The systemic and hematologic manifestations are generally absent when the lesion is still in the operable stage. At operation the presence of a soft, flat, infiltrating tumor strictly limited to the distal portion of the stomach, associated with a disproportionate number of large, succulent, isolated, adenoid-like glands, should suggest the possibility of a lymphogranulomatosis. The final diagnosis is a histologic one. In any case of inoperable tumor of the stomach in which the possibility of Hodgkin's disease is to be considered, biopsy should not be omitted.

Even when a careful exploration fails to demonstrate evidence of granulomatous tissue other than that extirpated, a guarded prognosis should be made. Gross lesions in inaccessible regions and microscopic involvement of the structures examined at the operating table may coexist without the possibility of detection. When the extent of involvement precludes resection, the patient should be given the benefit of roentgen therapy.

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24. Since the completion of this manuscript my attention was directed to an article by Dr. V. C. David (Pseudocarcinoma of the Stomach, Ann. Surg. **87**:555 [April] 1928), in which he describes a woman, aged 50, who had suffered from abdominal complaints for three months and who presented roentgen evidence of a filling defect of the antrum. A preoperative diagnosis of carcinoma of the stomach was made. The gastric tumor which was resected by Dr. Dean Lewis proved microscopically to be lymphogranulomatous. The report stated that subsequently enlarged glands developed, which receded under roentgen treatment, following which a rectal mass, presumably a Hodgkin's infiltration, appeared. A personal communication from Dr. Dean Lewis indicates that no lesion other than the one in the stomach was demonstrable at the time laparotomy was performed and that for over two years no other evidence of Hodgkin's disease could be detected.

THE ETIOLOGY AND PATHOLOGY OF CYSTS OF THE PANCREAS *

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In a previous communication [1] we reported on a clinical study of forty-seven cases of pancreatic cysts treated surgically at the Mayo Clinic in the last ten years. In this paper we shall consider: (1) the pathogenesis of cysts of the pancreas, (2) our classification and (3) the pathologic manifestations of such cysts. As a basis for our study, we reviewed the literature, the records at the clinic and the operative and necropsy material obtained in eighty-eight cases of cysts of the pancreas treated surgically, as well as that in twenty cases in which such cysts were discovered incidentally at necropsy.

Comparatively little experimental work has been done on the production of cysts in the pancreas. Senn [2] ligated the pancreatic duct in dogs but was unable to produce a cyst, although it appeared that ectasia of the duct followed the ligation. He concluded that factors other than mere obstruction were instrumental in the production of cysts. He suggested that the secretion failed to absorb. Thiroloix [3] ligated the accessory pancreatic duct in the dog and injected 7 cc. of a mixture of soot and phenolized liquid petroleum into the duct of Wirsung. The vertical part of the gland was removed. A large cyst was found in the splenic portion of the gland when the animal was killed almost three months later. This cyst contained clear fluid and hard irregular calculi of about 1 mm. in diameter. Lazarus [4] crushed the pancreas of a dog and produced a hematoma. Six weeks later a cyst "the size of a goose egg," which contained a milky fluid, was found. Binet and Brocq [5] injected

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* Work done in the Section on Pathologic Anatomy, the Mayo Clinic.

1. Judd, E. S.; Mattson, Hamlin; and Mahorner, Howard R.: Pancreatic Cysts: Report of Forty-Seven Cases, Arch. Surg. **22**:838 (May) 1931.

2. Senn, Nicholas: The Surgery of the Pancreas as Based upon Experiments and Clinical Researches, Am. J. M. Sc. **92**:141 (July) 1886; **93**:121, 1887; Experimental Surgery, Chicago, W. T. Keener, 1889.

3. Thiroloix, J., quoted by Oser: Diseases of the Pancreas, in Nothnagel: Encyclopedia, Philadelphia, W. B. Saunders Company, 1903.

4. Lazarus, Paul: Beitrag zur Pathologie und Therapie der Pankreaserkrankungen mit besonderer Berücksichtigung der Cysten und Steine, Ztschr. f. klin. Med. **51**:95 and 203, 1904; **52**:146 and 381, 1904.

5. Binet, Léon; and Brocq, Pierre: Réproduction expérimentale de la pancréatite hémorrhagique avec stéato-nécrose et du pseudo-kyste pancréatique par l'injection de sels de calcium dans le canal de Wirsung, Compt. rend. Soc. de biol. **83**:341 (March) 1920.

a solution of calcium chloride into the duct of Wirsung of a dog and produced acute hemorrhagic pancreatitis, and in one instance a pseudocyst. They concluded that the reaction resulted from the activation of the trypsinogen by the calcium chloride, since it did not follow the injection of a solution of sodium fluoride. Opie [6] called attention to the relationship between diseases of the pancreas and the obstruction of the normal outflow of bile by a stone in the common bile duct. Archibald [7] found that bile injected into the pancreatic duct produced pancreatitis; if the bile was infected, the results were more marked.

It may be said that most of the experimental evidence concerning the production of cyst of the pancreas is inconclusive. Yet the results, when correlated with clinical observations in man, throw light on the manner in which certain of these cysts are formed.

After a study of the different types of cysts of the pancreas, we made a classification which is based on their etiology:

I. Cysts resulting from defective development
  (1) Cysts in infants
  (2) Cysts associated with polycystic disease of the kidney
  (3) Dermoid cysts
  (4) Inclusion cysts
II. Cysts resulting from trauma
III. Retention cysts
IV. Neoplastic cysts
  (1) Cystadenoma
  (2) Cystadenocarcinoma
  (3) Teratomatous cysts
V. Cysts resulting from parasites

CYSTS RESULTING FROM DEFECTIVE DEVELOPMENT

Cysts in Infants.—Fault of development of an acinus or a duct in some instances apparently plays a part in the formation of cysts of the pancreas. Such cysts are found rarely in infants. Connolly [8] reported a case in a child aged 14 months. Railton [9] reported a case of pancreatic cyst in a child aged 6 months, and Eha [10] reported a case in an infant

6. Opie, E. L.: The Relation of Cholelithiasis to Disease of the Pancreas and to Fat Necrosis, Am. J. M. Sc. **121**:27 (Jan.) 1901; Diseases of the Pancreas, Philadelphia, J. B. Lippincott Company, 1910.

7. Archibald, E.: The Experimental Production of Pancreatitis in Animals as the Result of the Resistance of the Common Duct Sphincter, Surg. Gynec. Obst. **28**:529 (June) 1919.

8. Connolly, D. I.: Note on a Case of Pancreatic Cyst in a Child Aged 14 Months, Lancet **1**:803, 1911.

9. Railton, T. C.: A Case of Pancreatic Cyst in an Infant, Brit. M. J. **2**:1318, 1896.

10. Eha, C. E.: Case of Congenital Pancreatic Cyst, J. A. M. A. **78**:1294 (April 29) 1922.

aged 5 months. He thought that the cyst was congenital. The part that trauma at birth may have played cannot be overlooked.

Cysts of the Pancreas Associated with Polycystic Disease of the Kidney.—Cysts of the pancreas, like those of the liver, are sometimes associated with polycystic disease of the kidneys. In one of our necropsy cases, bilateral polycystic kidneys, multiple cysts in the liver and a few cysts in the head and the adjacent part of the body of the pancreas, of from 1 to 2 mm. in diameter, were found. These cysts were thin-walled and contained clear fluid. They were lined with a single layer of cuboidal epithelium. Kaufmann [11] also observed cysts in the pancreas associated with polycystic disease of the kidneys. Judd [12] found a congenital cystic kidney at an operation that was performed for cyst of the pancreas.

Dermoid Cysts.—In the pancreas, dermoid cysts are rare. One was removed successfully by Judd; the case was reported in detail by Masson and Caylor.[13] Another case was reported by Dennis.[14] These cysts contain hair and caseous material, and microscopically the walls show the picture characteristic of dermoid cysts (fig. 1).

Inclusion Cysts.—These cysts have developed in an organ from cells which are not normally there, but which were incorporated in the organ from some extraneous tissue by a fault of development in embryonal life. The remote possibility that such cysts may be present in the pancreas should not be overlooked. Carling and Hicks [15] expressed the belief that certain true cysts of the pancreas are the result of inclusions of portions of the wolffian body.

CYSTS RESULTING FROM TRAUMA

Injury to the abdomen precedes the development of cysts of the pancreas with significant frequency in the various series of cases reported in the literature. Some patients give a definite history that the mass developed directly following injury. These facts, together with the experimental evidence produced by Lazarus, point to trauma as a factor in the development of certain cysts of the pancreas.

The term pseudocyst is found in the literature and is intended to include extraparenchymal or interparenchymal cysts, which are not and

11. Kaufmann, Eduard: Lehrbuch der speziellen pathologischen Anatomie, Berlin, Walter de Gruyter & Company, 1922; Pathology for Students and Practitioners, Philadelphia, P. Blakiston's Son & Company, 1929.

12. Judd, E. S.: Cysts of the Pancreas, Minnesota Med. **4**:75 (Feb.) 1921.

13. Masson, J. C., and Caylor, H. D.: Dermoid Cyst of the Pancreas, Surg. Clin. North America **9**:837 (Aug.) 1929.

14. Dennis, W. A.: Dermoid Cyst of the Pancreas, Surg. Clin. North America **3**:1319 (Oct.) 1923.

15. Carling, E. R., and Hicks, J. A.: A Consideration of Two Cases of Cystadenoma of the Pancreas and Their Probable Relationship to Polycystic Conditions Found in Other Viscera, Brit. J. Surg. **13**:238 (Oct.) 1925.

which were not at any time in their development lined with epithelium. Practically, it is impossible to distinguish true cysts and pseudocysts, because true cysts sometimes lose their epithelial lining; they are then in no way different, morphologically, from cysts that are traumatic in origin.

Lloyd [16] reported two cases of cyst of the pancreas with the observations at operation, and called attention to the fact that many of the so-called hemorrhagic cysts of the pancreas are in reality hemorrhages into the lesser peritoneal cavity. The two cysts that he reported were undoubtedly of traumatic origin, and yet he recovered trypsinogen from

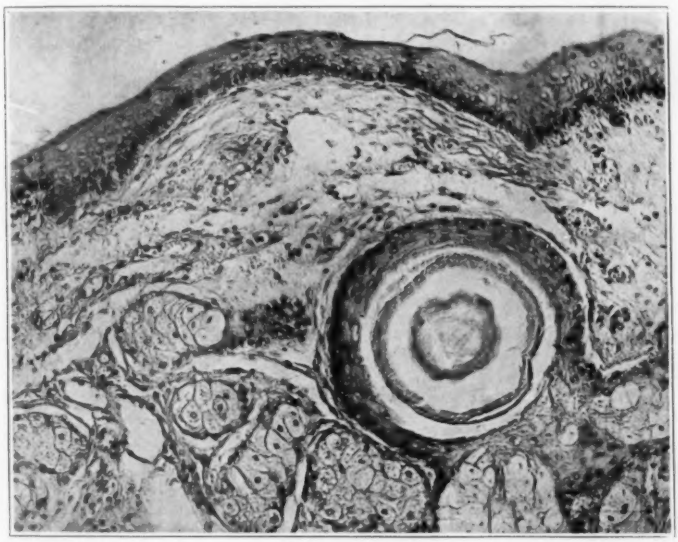

Fig. 1.—Wall of a dermoid cyst of the pancreas (case reported by Masson and Caylor).

the fluid that drained from them. Warnock [17] reported the case of a boy, aged 7 years, in whom a mass developed in the upper part of the abdomen after severe trauma. At operation a pancreatic cyst was found. Such cases leave little doubt that trauma causes cysts. Of the one hundred and nineteen cases reviewed by Körte,[18] there was a definite history of injury in thirty-three (28.2 per cent). In Judd's series there was a

16. Lloyd, Jordon: Injury to the Pancreas: A Cause of Effusions into the Lesser Peritoneal Cavity, Brit. M. J. **2**:1051, 1892.

17. Warnock, H. A.: Pseudocyst of the Pancreas, Brit. M. J. **1**:104 (Jan. 19) 1929.

18. Körte, Werner: Die chirurgischen Krankheiten und die Verletzungen des Pankreas, Stuttgart, Ferdinand Enke, 1898.

history of trauma in 2.4 per cent, and in McWhorter's [19] series 15.7 per cent of the patients gave a history of abdominal injury.

In the forty-seven cases of cyst of the pancreas in which surgical procedures had been carried out at the Mayo Clinic since Judd's report in 1921, there was a history of trauma preceding the onset of symptoms in eight (17 per cent).

A man, aged 27, was struck in the abdomen in an automobile accident a month before the onset of pain and swelling in the left part of the abdomen. Eight hundred cubic centimeters of straw-colored fluid was drained from a benign cyst five months after the accident. The discharge continued for three months; then the wound closed, and the patient recovered uneventfully.

In a case of fracture of a cervical vertebra from a fall, the patient, a man, aged 65, began to feel fulness in the left upper part of the abdomen six years later; this continued for twenty years. Operation was performed, and a malignant pancreatic cyst was found.

A woman, aged 63, had fractured two ribs in a fall six months before the beginning of symptoms. One year after the accident a laparotomy was performed, and a pancreatic cyst was found. The pancreas was hard and nodular, and a malignant lesion was suspected. The patient died elsewhere six months after the operation. We did not obtain further information.

A farmer, aged 30, was struck in the right side of the abdomen by a steering wheel. Three days later he noticed abdominal swelling. Operation was performed seven months after the accident, and a pancreatic cyst containing 1 liter of clear fluid was drained.

A woman, aged 40, suffered a blow in the upper part of the abdomen in a railroad wreck. Examination at the clinic, almost a year after the accident, disclosed an epigastric mass. On exploration, the mass proved to be a pancreatic cyst which contained about 1 liter of hemorrhagic fluid.

A patient, aged 41, was struck in the abdomen in an automobile accident. An emergency operation was performed at once elsewhere, and about 4 liters of clotted blood was removed from the abdomen. Yellowish fluid discharged intermittently from a sinus. Three months after the accident the abdomen was explored, and about 1 liter of cloudy fluid was drained from a cyst which apparently was attached to the pancreas.

In another case, a man, aged 41, tripped and fell while he was running; he remained unconscious for five minutes. He bled profusely from the nose, and vomited. The abdomen was painful and rigid. The upper part of the abdomen became enlarged and remained so. About 6 liters of bloody fluid was drained from a pancreatic cyst thirty-eight days after the accident.

A patient, aged 25, was in an automobile which turned over three times. The sixth, seventh and eighth ribs on the left side were fractured, and the patient was unconscious for six hours. Six days later he noticed a mass in the left upper part of the abdomen. At operation, a cyst of the pancreas was found.

In many cases of cyst of the pancreas following trauma, symptoms do not develop for weeks or months, although sometimes they appear at once. It is difficult to interpret the signficance of such a long latent period. It is possible that cysts grow by the mere accretion of fluid due

19. McWhorter, G. L.: Cysts of the Pancreas, Arch. Surg. **11**:619 (Oct.) 1925.

to a difference in the osmotic pressure. Perhaps after injury to the pancreas and the first hemorrhage, the ferments erode the tissue, causing further hemorrhage and thus enlargement of the cyst.

The history in some cases suggested that trauma may be more indirect and still produce cysts. McCann,[20] Carslaw,[21] Mayo[22] and Russ[23] reported cysts of the pancreas that were observed during pregnancy or shortly after parturition. In three of eighty-eight cases in which the operation was performed at the clinic, the cyst of the pancreas was discovered during pregnancy or shortly after parturition. In two cases the gallbladder contained stones. The rupture of a vessel during the strain of parturition suggests itself as one possible method by which a cyst may develop. Russ supposed that in the case which he reported a hemorrhagic lesion occurring during the course of puerperal sepsis was the cause of the cyst. This brings up the possibility of the production of a cyst of the pancreas by an embolism, which, either sterile or infected, might produce necrotic areas subject to the action of the escaped pancreatic ferments, with consequent sepsis, hemorrhage and the formation of a cyst.

RETENTION CYSTS

The part played by obstruction to the outflow of pancreatic secretion in the production of cysts is not well defined. Virchow,[24] in 1863, described uniform or irregular rosary-like dilatation of the pancreatic duct, which he termed pancreatic ranula. We have observed in a necropsy specimen an irregular dilatation of the duct distal to an area of stenosis produced by carcinoma in the head of the pancreas. Ligation of the pancreatic duct does not result in the formation of cysts, and there is little if any, dilatation distal to the point of ligation. Attention has been called to the fact that theoretically partial and not complete obstruction results in hydronephrosis and in dilatation of the biliary passages, and that this may likewise be applied to the pancreas. Virchow noted that pancreatic calculi are sometimes found in cysts of the pancreas, and he likened them to the calculi found in sublingual ranula. There were pancreatic calculi in only one of the cases in our series. It may be that gallstones lodged in the termination of the common bile duct obstruct the outflow of pancreatic fluid, thus acting as a factor in the production

20. McCann, F. J.: A Large Pancreatic Cyst Simulating an Ovarian Tumor, Proc. Roy. Soc. Med. **4**:235, 1912-1913.

21. Carslaw, R. B.: Acute Pancreatitis Followed by Development of a Pancreatic Cyst; Recovery, Lancet **2**:132 (July 16) 1921.

22. Mayo, W. J.: Pancreatic Cyst, Med. Rec. **45**:168 (Feb.) 1894.

23. Russ, W. B.: Pseudocyst of Pancreas Apparently Due to Hemorrhagic Necrosis Occurring During the Course of a General Sepsis, J. A. M. A. **77**:620 (Aug. 20) 1921.

24. Virchow, Rudolf: Die krankhaften Geschwülste, Berlin, August Hirschwald, 1863, pp. 276-277.

of cysts. Durante [25] described a cyst which enclosed a softened pancreas; *Ascaris lumbricoides* occluded the pancreatic duct.

More interesting than the mere passive rôle of obstruction is the possibility that gallstones in the end of the common bile duct may shunt bile into the pancreatic duct. Binet and Brocq, Opie and Archibald have shown that acute hemorrhagic pancreatitis may be brought about by the influx of bile in the pancreatic ducts. Perhaps the reaction in acute hemorrhagic pancreatitis and the injury of the tissues proceed to lysis, isolation of the fluid and the formation of a cyst. Münzer [26] considered the question of the formation of cysts by softening and even the softening occasioned in fat necrosis. The softening resulting from an infarct, or the reaction to an infected embolus, may contribute in a similar manner to the production of a cyst. Cysts that owe their origin to hemorrhage into the tissue (apoplectic cysts) and to softening are pseudocysts and are not lined with epithelium. Lloyd and Israel [27] observed a necrotic pancreas floating as a sequestrum in a cyst of the organ.

Tilger [28] advanced the theory that retention and obstruction to the outflow of secretion is brought about by the fibrosis following chronic interstitial pancreatitis. He observed that the ducts and acini appeared to be snared off by proliferation of the interstitial connective tissue. We have seen microscopic appearances suggesting such a method of formation (fig. 2). We have found fields in which the interstitial connective tissue separated small, individual, microscopic cysts quite definitely. Yet even in the same glands in which we have observed these appearances, there was only focal fibrosis. Moreover, in a pancreas in which there is much interstitial fibrosis there may be no evidence of the formation of the cysts. We have seen strikingly little fibrosis in glands containing simple cysts.

NEOPLASTIC CYSTS

The term "proliferation cyst" is encountered frequently in the literature, and such cysts are included under neoplasms in our classification. Neoplasms of the pancreas produce cysts in two ways: by an inherent tendency in the growth to form a cyst lined with epithelium or by degeneration and liquefaction in the tumor. Carcinoma of the pancreas, although relatively common, does not have a tendency to develop cysts. However, in such a tumor we have observed microscopic cysts lined with epithelium.

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25. Durante, F.: Cisti da ritenzione del pancreas, Arch. ed atti d. Soc. ital. di chir. **9**:109, 1894; abstr., Zentralbl. f. Chir. **21**:424 (April) 1894.

26. Münzer, Max: Pankreascysten, Centralbl. f. d. Grenzgeb. d. Med. u. Chir. **6**:490, 573 and 664, 1903.

27. Israel, O.: Zwei Fälle von Necrose innere Organe bei Diabetes Mellitus, Virchows Arch. f. path. Anat. **83**:181 (Jan.) 1881.

28. Tilger, Alfred: Beitrag zur pathologischen Anatomie und Aetiologie der Pancreas-Cysten, Virchows Arch. f. path. Anat. **137**:348 (July) 1894.

Cystadenoma.—Ewing [29] stated that adenomas of the pancreas are somewhat rare, and adenomas in which cysts form must, of course, be even more rare. The meager descriptive detail of the gross and microscopic appearances of some cysts reported in the literature as cystadenomas makes it difficult to accept many of them as true neoplasms. This fact has been emphasized by Fitz.[30] Multilocular cysts are not necessarily cystadenomas. Even in benign cysts there may be papillary ingrowths or cysts in the wall. Residual pancreatic tissue has been described in the walls of pancreatic cysts, and we have observed it also (fig. 3). There is a possibility that this tissue, isolated as it is from

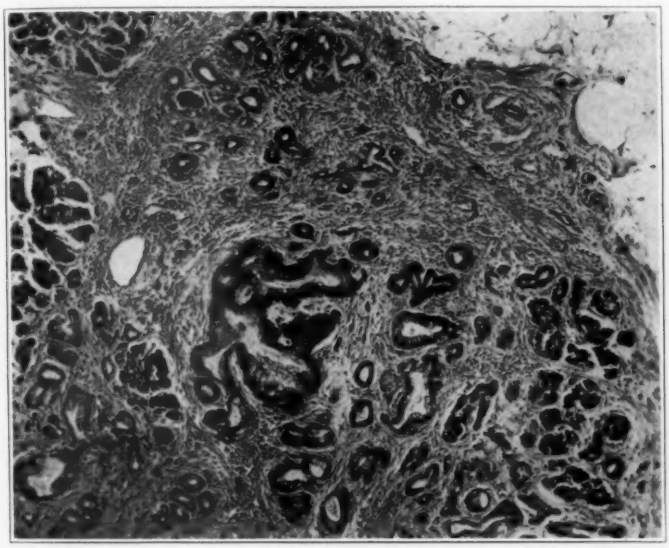

Fig. 2.—Interstitial tissue apparently snaring off acini and thus forming retention cysts.

the pancreatic ducts, might give rise to retention cysts. Körte reviewed from the literature thirteen cases of proliferative cysts of the pancreas. In 1902, Fitz reviewed eight cases of cystadenoma and added one of his own. Malcolm [31] described a cystic tumor of the pancreas that probably was a true neoplasm. There were many cysts in the tumor that were lined with epithelium. Kaufmann also reported a true cystadenoma of the pancreas.

29. Ewing, James: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1929.

30. Fitz, R. H.: Multilocular Cystoma of the Pancreas, Am. J. M. Sc. **120**: 184 (Aug.) 1900.

31. Malcolm, J. D.: A Case of Complete Removal of a Multilocular Cystic Tumor of the Pancreas, Lancet **1**:1676, 1906.

Only two cases of cystadenoma of the pancreas were found among the eighty-eight cases of cyst of the pancreas in which operation was performed at the Mayo Clinic and in the twenty cases noted at necropsy. In one of the cases a cyst had been drained in January, 1921. The pathologist reported cystadenoma. Between January, 1921, and March, 1923, the patient was operated on six times for cysts of the pancreas. The mass recurred in the form of multiple cysts containing a milky, or a thick, mucilaginous fluid. The patient died elsewhere on June 9, 1926, and we were unable to obtain any further information concerning the lesion. The second patient with benign cystic tumor of the pancreas came to necropsy. This patient died eleven days after an operation at

Fig. 3.—Residual pancreatic tissue in the fibrous wall of a simple multilocular cyst of the pancreas.

which a large pancreatic cyst was drained. At necropsy it was found that the cystic tumor was fused to the head of the pancreas; it measured 12 by 12 by 7 cm., and the cavity, which made up about two thirds of the bulk of the mass, was lined with a necrotic, shreddy material, and had a capacity of about 400 cc. Microscopic examination of sections from the main body of the tumor and from the wall of the cyst disclosed a cellular structure not unlike the normal pancreas; the epithelial cells were arranged into acini and ductlike structures, and there was little interparenchymal connective tissue (fig. 4).

Cystadenocarcinoma.—Malignant cysts of the pancreas are likewise rare. Scotti [32] reported on a cystic tumor of the pancreas with lymphatic

32. Scotti, G.: Adeno-Cistoma papillefero del pancréas, Arch. per le sc. med., 1906; abstr., Centralbl. f. allg. Path. u. path. Anat. **18**:844 (Oct.) 1907.

and pulmonary metastasis and implantations on the peritoneal surface. Hartman [33] reported observations at necropsy in a case of malignant cystic tumor of the pancreas with metastasis to the liver.

Among the eighty-eight patients with pancreatic cyst treated surgically at the Mayo Clinic, there were four with carcinomatous cysts. In one case a large cystic tumor was found with nodules over its surface and nodules in the liver in the left side of the abdomen. Two of the nodules of the liver were excised and proved to be carcinoma. The surgeon thought that the cystic tumor originated in the pancreas. In the second case there was a cystic mass of the pancreas approximately 20 by 25 cm. Part of the mass removed at operation proved to

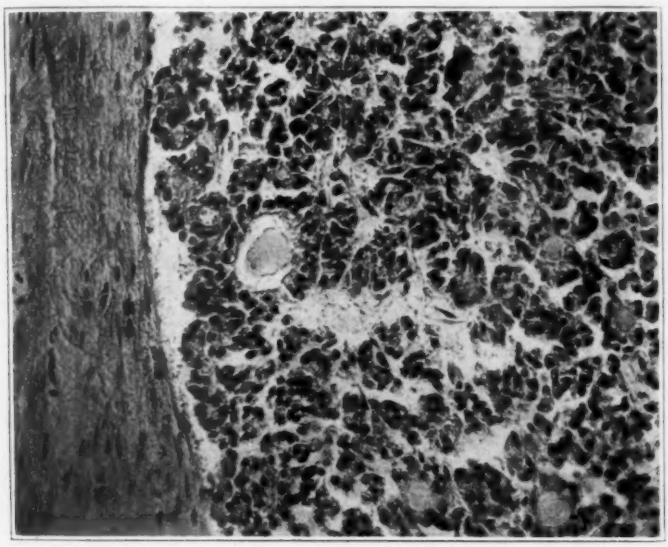

Fig. 4.—Wall of cyst in cystadenoma of pancreas (hematoxylin and eosin; × 175).

be benign. However, tissue removed from other cystic masses in the same pancreas was reported as cystadenocarcinoma. The patient recovered from the operation, but we have no further information concerning the case. In the third case a large cystic tumor was removed from the tail of the pancreas. The cyst contained about 4 liters of fluid, and its inner walls were irregular and lined with necrotic, shreddy tissue in which there were degenerated epithelial cells that appeared to be malignant. In one part of the mass was a solid tumor; the cyst was directly contiguous with it. Microscopically, the tumor was carcinoma of the pancreas. Part of the wall of the cyst was smooth externally

33. Hartman, M.: Kystes du pancréas, Rev. d. chir. **11**:409, 1891.

and consisted of connective tissue. In the fourth case, a pancreatic cyst was drained surgically, and the patient died following the operation. The surgeon made a note at the operation that the pancreas was very hard. At necropsy a cyst of about 10 cm. in diameter was found in the lesser peritoneal cavity. It was filled with straw-colored fluid and was adherent to the pancreas, from the head to the tail. Carcinoma was found in the pancreas.

Teratomatous Cysts.—Kerr [34] reported a cyst, the wall of which he said was teratomatous. He did not give a detailed description of the histopathologic features.

CYSTS RESULTING FROM PARASITES

Cysts of the pancreas caused by parasites are rare. They are encysted forms of some of the parasites for which man is the intermediate host. We have seen only two types described, echinococcus cyst and *Cysticercus cellulosae*.

Hanser,[35] in 1912, reviewed twenty-eight cases of echinococcus cyst noted in the literature. Twenty-two of these were in the pancreas and six were in the vicinity of the pancreas. Seyfarth,[36] in 1920, reviewed forty cases of echinococcus cyst of the pancreas.

The pathologic diagnosis rests on the finding of scolices or hooklets (Stitt,[37] Rivas [38]). Echinococcus cysts may be very large. Railliet and Monot [39] stated that *Cysticercus cellulosae* have been found in the pancreas of man. Such systs are small, about 15 by 7 mm. in diameter, and contain the scolex and hooklets of *Taenia solium*.

GENERAL CHARACTERISTICS OF CYSTS OF THE PANCREAS

Shape.—Very small cysts are spherical. Larger cysts are shaped by their surroundings. Extremely large cysts assume ameboid characteristics and may fill the entire abdomen. Certain cysts are multilocular (fig. 5); although they are rounded on the outside, they have many partially or completely separated spaces within.

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34. Kerr, A. A.: Cysts and Pseudocysts of the Pancreas, Surg. Gynec. Obst. **27**:40 (July) 1918.

35. Hanser, Robert: Ueber Echinokökken des Pankreas, Beitr. z. klin. Chir. **77**:360, 1912.

36. Seyfarth, Carly: Parasiten im Pankreas, Centralbl. f. Bakteriol. **85**:27 (Sept.) 1921.

37. Stitt, E. R.: The Diagnostics and Treatment of Tropical Diseases, ed 5, Philadelphia, P. Blakiston's Son & Company, 1929.

38. Rivas, Damaso: Human Parasitology, Philadelphia, W. B. Saunders Company, 1920.

39. Railliet and Monot: Ascaride dans le pancréas d'un process, Compt. rend. Soc. de biol. **45**:407 (April) 1893.

Size.—The size of pancreatic cysts varies within wide limits. The largest one reported in the literature contained 20 liters of fluid.[40] Most of the cysts reported were large enough to be palpated through the abdominal wall. In one of the forty-seven cases that we reported it was estimated that 20 liters of fluid was present; in one case 8 liters of fluid was present; in one, 6 liters; in two, 4 liters each, and in two, 3 liters each. The smallest cyst for which operation was performed in our series was 6 cm. in diameter. It originated in the head of the

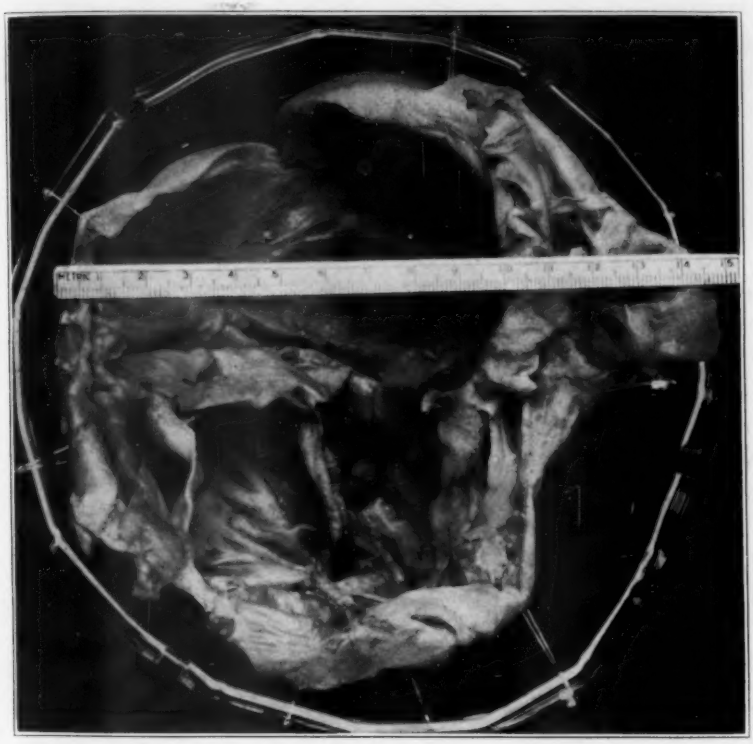

Fig. 5.—Multilocular simple cyst of the pancreas.

pancreas and presented in the transverse mesocolon. The duct of Wirsung and the cyst both contained stones. Three other small cysts found in this series were 7, 8 and 9 cm. in diameter, respectively, and each was enucleated completely.

Very small cysts are sometimes found at necropsy (fig. 6). In the necropsy records of the clinic we were able to find only twenty cases of cysts of the pancreas that had not been operated on. The small cysts

40. Stapper, Julius: Beiträge zur Diagnose der Pancreascysten, Bonn, Joseph Bach, 1892.

Fig. 6.—Numerous small thin-walled cysts throughout the pancreas.

that were found at necropsy usually contained clear fluid; their walls were thin and microscopically consisted of connective tissue and an epithelial lining. It is of historic interest that Klebs [41] gave the name "acne pancreatica" to cases in which the contents of the cysts had become mushy. Generally only a single layer of epithelial cells lines these cysts. They vary from the tall columnar (fig. 7) to the flattened type. Sometimes there are little papillary projections into the cavity of the cyst (fig. 8). Such projections do not indicate that the cyst itself is a neoplasm or that it is a cystadenoma.

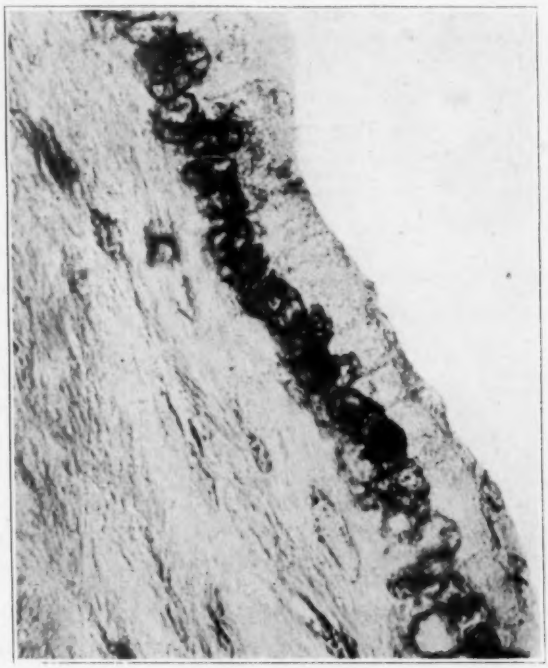

Fig. 7.—Columnar epithelial cells lining simple cyst of the pancreas (× 700).

Number.—In twelve of the twenty cases in our series that were noted at necropsy for which operation had not been performed, the cysts were multiple; in seven cases the cysts were single and in one case, multilocular. Our information concerning the number, type and pathologic change in the larger surgical cysts is limited, because extensive exploration frequently is impossible, and few cases come to necropsy.

Site.—In the cases noted at necropsy four cysts were described as being confined to the tail of the pancreas (three single and one multiloc-

41. Klebs, Edwin: Handbuch der pathologischen Anatomie, ed. 2, Berlin, A. Hirschwald, 1876.

ular), three were in the head only (two single and one multiple), and three were in the body (two single). In the remaining ten cases the cysts were found throughout the gland in two cases, in the head and body in two, and in the tail and body in one case; in five cases the site was not adequately described. This distribution of the cysts is not indicative of a place of predilection for pancreatic cysts. It was Lazarus' belief that the least common site was in the head of the pancreas because of the least likelihood of retention. Körte gave the site in forty-seven cases as follows: the head in sixteen cases, the body in seven, the body and tail in twelve and the tail in twelve.

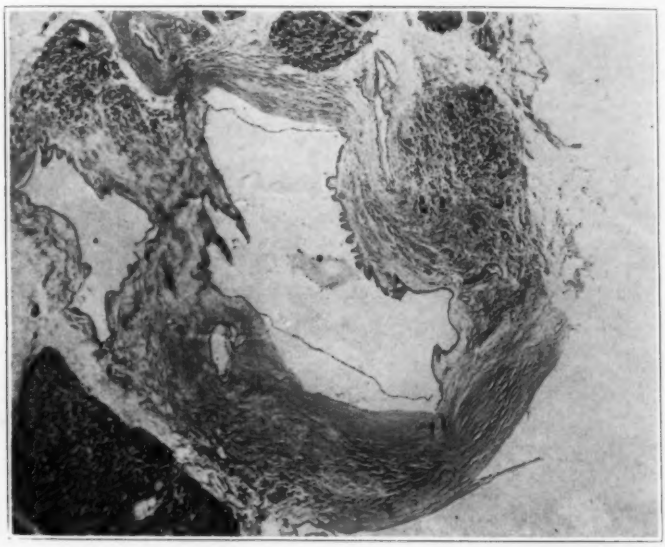

Fig. 8.—Simple cyst of pancreas, showing papillary projections (hematoxylin and eosin; × 20).

Content.—The gross appearance of the contents of pancreatic cysts is variable. The fluid was clear or amber-colored in only seven of our series of forty-seven cases. In fourteen cases it was chocolate-colored or blood-stained, and in nine cases the contents were described as: cloudy fluid and gelatinous material; yellow milky fluid; thick, oily, bloody material; cloudy fluid; clear gelatinous fluid (subsequently thick mucilaginous and later milky), light-colored honey-like material, yellowish-green fluid, slightly turbid fluid, or greenish-black fluid. The appearance of the contents in the remaining seventeen cases was not described.

Sometimes the bloody appearance of a hemorrhagic cyst disappears, and the contents become clear fluid. Lazarus observed this in his experimentally produced cyst, and this seems to have taken place in one of the

cases in our series in which the condition followed trauma. The patient was a man, aged 27, who had suffered a blow in the abdomen in an automobile accident five months before admission. He was operated on, and a cyst of the pancreas was found which was estimated to be 24 cm. in diameter and to contain about 800 cc. of a straw-colored fluid. It had been aspirated five times before he came to the clinic. Amber-colored fluid was removed each time. Histologic examination of the walls of cysts sometimes shows a blood pigment which indicates their hemorrhagic origin, whether or not their contents are clear. Dermoid cysts of the pancreas, like those in other parts of the body, contain a grumous, cheesy material and hair, and they may even contain teeth. Degenerated and necrotic tissue may sometimes be found in cysts, and even portions of the pancreas.[42]

Microscopically, cysts may contain epithelial cells, erythrocytes, leukocytes, globules of fat, crystals of fatty acids, cholesterol, hematin crystals and necrotic tissue.[43] Serum albumin, serum globulin, mucin, peptone, hemoglobin, leucine, tyrosine and sugar also have been found.[44] The reaction usually is alkaline. The content of a cyst removed by Bozeman [45] and described by Garrigues [46] was acid. The specific gravity varies from 1.007 (Treamaine) [47] and 1.009 (Morton) [48] to 1.060, which is that of blood. Ferments are often present. In the fluids in sixty-six cases in Körte's series, in which the contents were analyzed in this regard, twelve were found not to contain ferments, twenty were found to contain one ferment (fourteen starch-splitting, three fat-splitting, and three protein-splitting), twenty were found to contain two ferments (sugar and fat, fourteen, sugar and protein, four, and fat and protein, two), and fourteen were found to contain three ferments. The presence of a starch-splitting ferment is not pathognomonic of pancreatic cysts, since either isolated or free fluids in the abdominal cavity may contain it.[49]

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42. Lloyd (footnote 16). Israel (footnote 27).

43. Lazarus (foonote 4). Opie (footnote 6). Oser, Leopold: Diseases of the Pancreas, in Nothnagel: Encyclopedia, Philadelphia, W. B. Saunders Company, 1903, pp. 17-270. Pepper, William: Tumour of the Head of the Pancreas, Am. J. M. Sc. **61**:159 (Oct.) 1871.

44. Lazarus (footnote 4). Körte (footnote 18).

45. Bozeman, N.: Removal of a Cyst of the Pancreas Weighing Twenty and One-Half Pounds, Med. Rec. **21**:46 (Jan.) 1882.

46. Garrigues, H. J.: The Anatomy and Histology of Cyst of the Pancreas, Med. Rec. **21**:286 (March) 1882.

47. Treamaine, W. S.: Cyst of the Pancreas Successfully Removed, Tr. Am. Surg. A. **6**:557, 1888.

48. Morton, B. B.: A Case of Pancreatic Cyst Associated with Glycosuria and Gallstones: Necropsy, Lancet **1**:242 (Jan.) 1897.

49. von Jaksch, R.: Ueber das Vorkommen von Fermenten in den Fäces der Kinder, nebst Bermerkungen über das Vorkommen von saccharificierenden Fermenten in Cysteninhalt, Ztschr. f. phys. Chem. **12**:116, 1888.

ETHYLENE ANESTHESIA

ANALYSIS OF REBREATHED MIXTURES *

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The carbon dioxide filter in inhalation anesthesia has been in use for several years, and analysis of the rebreathed gases has been made by F. T. Romberger and others on mixtures in which ether was used. However, no data have been published on patients in whom ethylene-nitrous oxide-oxygen anesthesia, without ether, has been used. The following preliminary report on a small series of cases is submitted in order to call attention to the possibility of inducing anesthesia with ethylene and maintaining surgical relaxation without giving additional anesthetic agents, after the introduction of a filter that removes carbon dioxide from the expired gases. Such a method is apparently without danger, and brings about a large reduction in the cost of the anesthetic agents.

ANALYSIS OF REBREATHED MIXTURES

In a series of seven cases, analyses were made on the contents of the rebreathing bag during the progress of the anesthesia. For each case at least seven samples, and in some eight, were taken at intervals of five or seven minutes. These samples were drawn directly from the rebreathing bag into sample tubes over mercury. The tubes were of approximately 25 cc. volume and were closed at one end by a ground glass stopcock and at the other by a column of mercury, the height of which could be regulated by raising or lowering a reservoir of mercury. In each sample, the concentrations of oxygen, carbon dioxide and ethylene were determined by analysis, and the relative nitrous oxide concentration determined by subtracting the sum of the three from 100 per cent. In each instance, a completely closed system made this computation possible. No samples were taken until the patient had been under the anesthetic for at least ten minutes; it was estimated that at this time all nitrogen had been removed from the expired gases.

The method of analysis was that of Haldane and Henderson, in which a known amount of gas is passed repeatedly from a calibrated buret into the absorbing solutions and returned to the buret until a constant reading is attained. This transfer is accompanied by means of a reservoir of mercury which is raised or lowered at will. The absorbents used were sodium hydroxide for carbon dioxide,

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potassium pyrogallate for oxygen and, in some cases, bromine water, and in others, 20 per cent silver nitrate, for ethylene.

In five of the seven cases, the carbon dioxide filter was used. In these cases anesthesia was induced with a mixture of 40 per cent ethylene, 40 per cent nitrous oxide and 20 per cent oxygen before the filter was cut in. When the filter was not used, the patient received this mixture throughout the course of the anesthesia. After the filter had been cut in, patients were carried on the contents of the rebreathing bag alone for from one hour to one hour and twenty minutes. During this time no additional ethylene or nitrous oxide was administered and only sufficient oxygen was given to keep the bag inflated. This oxygen was given continuously throughout the course of the anesthesia, so that at no time was the rebreathing bag allowed to become deflated. This prevented any great and sudden variation of the concentration of gases in the system. These patients, although they received no additonal anesthetic, evidenced perfect surgical anesthesia with better relaxation than those with whom the filter was not used. This observation held true for a large number of patients other than those on whom analyses were made. Furthermore, in those patients with whom the carbon dioxide filter was not used and in whom anesthesia was induced and maintained by means of a continuous supply of the mixture of 40 per cent

TABLE 1.—*Results of Analysis of Rebreathed Mixture in Case 1*

Sample	O_2	CO_2	C_2H_4	N_2O
1	20.80	0.90	13.00	65.30
2	25.85	0.75	37.00	36.40
3	29.80	0.70	40.50	29.00
4	34.00	0.60	29.00	36.40
5	42.50	0.50	25.00	32.00
6	47.00	0.65	23.50	28.85
7	49.75	0.35	22.50	27.40

ethylene, 40 per cent nitrous oxide and 20 per cent oxygen, it was impossible to keep surgical relaxation by the administration of oxygen alone.

CASE 1.—A woman, aged 27, weighing 110 pounds (49.9 Kg.), was subjected to the following operations: curettage of the uterus, cauterization of the cervix, myomectomy and appendectomy. The preparation included: pantopon, one-sixth grain (0.01 Gm.); scopolamine, one four-hundredth grain (0.00016 Gm.) injected one hour before operation and repeated in thirty minutes, and procaine hydrochloride, 1 per cent, injected into the fascia and muscles. Anesthesia was started at 9:48, and the mixture was "40-40-20." The filter was cut in at 10:13. The first sample was taken at 10:13. Samples were taken every five minutes. For twenty-five minutes, 400 cc. of oxygen per minute was given, and 350 cc. per minute for the remainder of the time. The results of the analysis of the rebreathed mixture are given in table 1.

The pulse rate was 72. Respirations were 20 per minute. The skin was dry

CASE 2.—A man, aged 38, weighing 220 pounds (99.7 Kg.), underwent appendectomy. In preparation, he was given pantopon, one-sixth grain, and scopolamine, one four-hundredth grain, one hour before operation with repetition of the injections in thirty minutes. Anesthesia was started at 10:46, and the mixture was "40-40-20." The filter was cut in at 10:54. The first sample (tube) was taken at 10:54. Samples were taken every seven minutes, alternately from exhaling tube and bag. For the first two samples, 400 cc. of oxygen per minute was given; 600 cc. for the next four samples; 550 cc. for the last two samples. The results of the analysis of the samples are given in table 2.

The pulse rate was 72. The respirations were 20 per minute. The blood pressure was: systolic, 126; diastolic, 88. The skin was wet.

CASE 3.—In case 3, the filter was not used. A man, aged 21, weighing 142 pounds (64.4 Kg.), was operated on for excision of varicose veins of the spermatic cord. The preparation consisted of morphine, one-sixth grain, and scopolamine, one six-hundredth grain (0.0001 Gm.) one hour before operation, the injection being repeated in thirty minutes. Anesthesia was started at 8:05. Samples were taken every five minutes. The mixture was "40-40-20." Eleven per cent oxygen

TABLE 2.—*Results of Analysis of Rebreathed Mixture in Case 2*

Sample	O_2	CO_2	C_2H_4	N_2O
1	15.00	2.50	52.00	30.70
2	20.00	3.50	7.00	69.50
3	25.00	2.40	41.00	31.60
4	27.50	0.20	27.00	45.30
5	36.00	1.70	27.50	34.80
6	38.00	0.35	27.50	34.15
7	43.50	3.05	20.00	33.45
8	47.00	0.50	18.00	34.50

TABLE 3.—*Results of Analysis of Rebreathed Mixture in Case 3*

Sample	O_2	CO_2	C_2H_4	N_2O
1	20.00	0.60	42.00	37.40
2	20.00	1.20	41.50	37.30
3	20.00	0.65	42.00	37.35
4	22.00	0.60	42.00	35.40
5	21.00	1.00	53.50	24.50
6	20.00	1.00	53.50	25.50
7	21.50	0.90	53.50	24.10
8	21.50	0.70	53.50	24.30

TABLE 4.—*Results of Analysis of Rebreathed Mixture in Case 4*

Sample	O_2	CO_2	C_2H_4	N_2O
1	17.00	3.60	56.50	22.90
2	16.00	0.40	56.50	27.10
3	15.00	3.50	63.00	18.50
4	16.50	0.85	52.50	30.15
5	20.00	0.25	50.00	29.75
6	18.50	1.90	50.00	29.60
7	18.00	0.25	57.50	24.25
8	18.50	0.20	52.50	28.80

was given during the first five minutes; 20 per cent oxygen, during the remainder. The results of the analysis of the samples are recorded in table 3.

The pulse rate was 68; the respiratory rate was 16. The blood pressure was: systolic, 112; diastolic, 70. The skin was dry.

CASE 4.—A man, aged 19, weighing 170 pounds (77.1 Kg.), was operated on for closure of a colostomy. In preparation, morphine, one-sixth grain, and scopolamine, one four-hundredth grain, were given one hour preoperatively and repeated in forty minutes. Anesthesia was started at 9:41, and the mixture was "41-41-18." The filter was cut in at 9:54. The first sample (ex. tube) was taken at 9:54 Samples were taken every seven minutes, alternately from exhaling and inhaling tube. Eighteen per cent oxygen was used for induction, and 400 cc. of oxygen per minute after the filter was cut in.

The patient was frightened and excited before the induction of anesthesia. The pulse rate was from 116 to 160; the respirations numbered from 20 to 24 per minute. The blood pressure was: systolic, 114; diastolic, 68.

CASE 5.—In case 5, the filter was not used. A woman, aged 30, weighing 110 pounds (49.9 Kg.), underwent the following operations: Dilation and curettage of the uterus; cauterization of the cervix; a Baldy-Webster suspension; resection of a cyst of the left ovary, and appendectomy. The preparation consisted of pantopon, one-sixth grain, and scopolamine, one four-hundredth grain, given one hour preoperatively and repeated in thirty minutes. Anesthesia was started at 9:30. The first sample was taken at 9:52. Samples were taken every five minutes. The mixture was: 90 per cent nitrous oxide and 10 per cent oxygen for the first eighteen minutes; 500 cc. each of ethylene, nitrous oxide and oxygen per minute for the remainder of the anesthesia. The results of the analysis of the samples are given in table 5.

TABLE 5.—*Results of Analysis of Rebreathed Mixture in Case 5*

Sample	O_2	CO_2	C_2H_4	N_2O
1	20.00	2.00	43.00	35.00
2	20.50	2.00	55.50	22.00
3	21.50	1.50	54.50	22.50
4	21.50	1.10	53.50	23.90
5	21.50	1.10	40.00	37.40
6	22.00	1.50	50.00	26.50
7	22.00	1.25	55.00	21.75
8	22.00	1.55	54.50	21.95

TABLE 6.—*Results of Analysis of Rebreathed Mixture in Case 6*

Sample	O_2	CO_2	C_2H_4	N_2O
1	14.00	1.50	51.00	33.50
2 Tube broken				
3	17.50	0.40	47.50	34.60
4	16.50	0.40	56.50	26.60
5	16.50	0.30	55.50	37.70
6	15.00	0.45	55.50	29.05
7	19.50	0.20	43.00	37.30
8	21.00	0.85	39.50	38.65

The pulse rate was from 88 to 100; the respirations were from 12 to 16 per minute. The blood pressure was: systolic, 110; diastolic, 70. The respirations increased in volume, but not in rate.

CASE 6.—A man, aged 33, weighing 160 pounds (72.6 Kg.), underwent appendectomy. In preparation, he was given pantopon, one-sixth grain, and scopolamine, one four-hundredth grain, at 7:15, and the injections were repeated at 8:30. Anesthesia was started at 9:15, and the mixture was: 2 liters (2,000 cc.) each of nitrous oxide and ethylene and 1,000 cc. of oxygen per minute. The filter was cut in at 9:27. The first sample was taken at 9:27. Samples were taken every five minutes. From 9:27 on, 450 cc. of oxygen was used. The results of the analysis of the samples are given in table 6.

The patient was maintained in good condition, with no variation. The pulse rate was 80; the respiration rate, 28.

CASE 7.—A woman, aged 26, weighing 104 pounds (47.2 Kg.), underwent the following operations: lysis of pelvic adhesions and resection of an ovarian cyst. The preparation consisted of: pantopon, one-sixth grain, and scopolamine, one

four-hundredth grain. Anesthesia was started at 9:09, and the mixture was "42-42-16." The operation was begun at 9:20. The filter was cut in at 9:25, using 400 cc. of oxygen per minute. The first sample was taken at 9:25. Samples were taken every five minutes. The results of the analysis of the samples are given in table 7.

The condition of the patient was good. One per cent procaine hydrochloride was injected into the fascia and rectus muscle. The pulse rate was from 75 to 100; the respirations were from 15 to 20 per minute. The blood pressure was: systolic, 100; diastolic, 70.

COMMENT

A comparison of the gases in those cases in which the filter was not used with those in cases in which it was used shows marked difference in concentration. In the former, the oxygen concentration remained relatively constant at approximately the induction percentage, while in the latter there was a gradual rise or accumulation of oxygen. This increase was as high as 49 per cent in sample 8 of case 1 and 47 per cent

TABLE 7.—*Results of Analysis of Rebreathed Mixture in Case 7*

Sample	O_2	CO_2	C_2H_4	N_2O
1	17.00	0.25	47.50	35.25
2	24.50	0.20	47.80	27.50
3	24.50	0.20	47.80	27.50
4	24.50	0.10	7.00	68.40
5	22.50	0.50	5.00	72.00
6	24.50	0.18	4.60	70.72
7	45.40	0.01	39.80	14.79

in case 2. It is doubtful that the amounts of oxygen fed were responsible for such an increase, as the bag would empty rapidly if a reduction of a few cubic centimeters was made. In the cases in which the filter was used, the difference between the percentage of oxygen administered and the amount recovered from the rebreathing bag on analysis was far out of proportion to the metabolic rate of the patient. The least amount that could possibly be used in any case was 350 cc. per minute, while in case 2, 600 cc. was necessary. The average amount administered was between 400 and 500 cc.

In many samples in cases 3 and 5, in which the filter was not used, the carbon dioxide concentrations were lower than in case 2, in which the filter was used. This apparent discrepancy is easily explained by the fact that in case 2 alternate samples were drawn from the exhaling tube. As would be expected, these samples show high concentrations of carbon dioxide, but little variation of the other gases present.

In cases in which the filter was not used, the average ethylene concentration was higher than the nitrous oxide concentration, but in cases in which the filter was used the reverse was true. This seems to indicate

that nitrous oxide was preferred in the former, whereas ethylene was preferred in the latter.

The economical feature of this method including the use of a filter is evident. A patient consuming 800 cc. each of nitrous oxide and ethylene per minute and carried for an hour and a half with no additional anesthetic would represent a saving of 81,000 cc. each of ethylene and nitrous oxide gas.[1]

1. Additional work is in progress in which analysis is being made of the ethylene, nitrous oxide, oxygen and carbon dioxide content of venous and of arterial blood during the course of the anesthesia. These are in conjunction with similar analyses of the rebreathed gases.

THE EFFECT OF SPINAL ANESTHESIA ON ARTERIAL TONE*

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In a previous study [1] it was shown that the cardiac output in dogs under spinal anesthesia remained at a nearly normal level unless a marked diminution in blood pressure took place. The decrease in blood pressure came first and was usually of greater degree than the later decrease in the output of the heart. This sequence of events is just the opposite of that found in experimental traumatic shock and experimental hemorrhage.[2] It was believed that a further comparison of these states might throw light on the nature of the different types of shock. These subjects have received a great deal of study in the past fifteen years, but, so far as one can judge from the literature, many of our concepts as to their exact nature are vague and incomplete.

METHOD

Dogs were used. They received barbital (0.3 Gm. per kilogram) intravenously from one to two hours before the experiments were begun. Blood pressure was measured by means of a mercury manometer connected with a cannula in the carotid artery. Spinal puncture was done as previously described by us. The animals received spinocaine (a proprietary procaine preparation) from 1 to 3 cc.,[3] depending on the size of the dog and the height of the anesthesia desired.

Arterial tone was measured by means of recording inflow into the selected artery. This vessel—the femoral, the brachial or the carotid artery—was exposed for a distance of from 10 to 20 cm., care being taken not to injure the branches. The distal end of the exposed vessel was then cannulated, the cannula pointing toward the heart. A bull-dog clamp was placed on the artery first. The cannula was connected to a metal coil, which was immersed in a water bath the temperature of which was kept at 38 to 40 C. To the other end of the coil was attached a rubber tube, which was connected with an ordinary 50 cc. buret that was kept at

* Submitted for publication, July 7, 1930.

* From the Departments of Gynecology and Medicine of Vanderbilt University.

1. Burch, J. C., and Harrison, T. R.: The Effect of Spinal Anesthesia on the Cardiac Output, Arch. Surg. **21**:330 (Aug.) 1930.

2. Blalock, A.: Mechanism and Treatment of Experimental Shock; Shock Following Hemorrhage, Arch. Surg. **15**:762 (Nov.) 1927.

3. Pitkin, G. P.: Controllable Spinal Anaesthesia "Spinocaine," Brit. J. Anaesth. **6**:22, 1928.

a height of 2 meters above the table on which the animal was prepared. The system was filed with a warm saline solution, care being taken to expel all the air. When a measurement of perfusion rate was to be made, the clamp at the end of the cannula was removed, and simultaneously a second bull-dog clamp was placed on the artery at the proximal point of exposure. Care was taken to be certain that this proximal clamp was always placed at the same point on the artery. In large dogs the inflow period was fifteen seconds; in small dogs, because of the lesser inflow, periods of thirty seconds were employed. This method is similar to that employed by Cattell.[4]

The advantage of this reverse perfusion method that we have used consists primarily in the fact that at all times, except during the relatively few seconds of the perfusion periods, the perfused tissues are receiving a normal blood supply. Forward perfusion methods involve the disadvantage of ischemia in the tissues to be studied, and it is well known that lack of oxygen may cause changes in vascular caliber.[5]

TABLE 1.—*The Effect of Spinal Anesthesia on the Perfusion Rate*

Experiment Number	Average Perfusion Rate, Cubic Centimeters per Minute: Before Spinal Anesthesia	Average Perfusion Rate, Cubic Centimeters per Minute: After Spinal Anesthesia	Region Perfused
29	66	94	Hind leg
31	83	104	Hind leg
32	49	145	Hind leg
44	60	100	Hind leg
46	67	50	Hind leg
33	15	28	Fore leg
36	19	44	Fore leg
34	92	95	Head
35	104	120	Head

In every instance several measurements of inflow were made. The values expressed in the tables are the averages of from three to five determinations and for convenience of comparison are expressed in terms of cubic centimeters per minute. Ordinarily, duplicate or triplicate measurements agreed fairly well, although considerable variations were observed in dogs with rhythmic fluctuations in blood pressure; it is thought that these variations represent changes in vasomotor tone.

RESULTS

The effect of spinal anesthesia on the perfusion rate is shown in table 1. In the first five of these experiments the anesthetized area, i. e., the posterior extremity, was perfused. In four of these marked increases in perfusion rate varying from 20 to 200 per cent were noted. In the fifth experiment, a diminution of about 25 per cent was found. We are unable to explain this exceptional observation.

4. Cattell, McKeen: Studies in Experimental Traumatic Shock: Action of Ether on Circulation in Traumatic Shock, Arch. Surg. **6**:69 (Jan.) 1923.

5. Krogh, A.: The Anatomy and Physiology of Capillaries, New Haven, Yale University Press, 1924.

Contrary to our expectations, it was found that the perfusion rate in the unanesthetized areas was also usually increased after spinal anesthesia. Presumably, this change is to be attributed to a slight diffusion toward the head of the anesthetic solution. It would appear that the vasomotor fibers are especially sensitive to the action of the anesthetic.

The observations reported in table 2 are of especial interest. In these animals a progressive drop in blood pressure was produced by repeated bleedings, and perfusion rates were measured at intervals throughout the experiments. In the first two experiments, the dogs

TABLE 2.—*The Effect of Hemorrhage on the Perfusion Rate*

	Before Hemorrhage		After Hemorrhage		
Experiment Number	Mean Blood Pressure, Millimeters of Mercury	Perfusion Rate, Cubic Centimeters per Minute	Mean Blood Pressure, Millimeters of Mercury	Perfusion Rate, Cubic Centimeters per Minute	Comment
42	138	49	120	35	No spinal anesthesia; hind leg perfused
			40	20	
			40	50	
			22	75	
			0	85	
43	118	160	104	80	No spinal anesthesia; hind leg perfused
			42	135	
			38	130	
			24	104	
32	52	144	38	141	Spinal anesthesia; hind leg perfused
44	82	100	90	96	Spinal anesthesia; hind leg perfused
			84	130	
			76	130	
			48	100	
46	94	46	76	46	Spinal anesthesia; hind leg perfused
			39	45	

had not received spinocaine. In each instance the initial hemorrhage was followed by a marked diminution in the perfusion rate, indicating arterial constriction. After the blood pressure had become very low—40 mm. of mercury or less—the perfusion rate increased toward or beyond the normal. It appears therefore that the initial effect of diminished blood volume is to cause a compensatory increase in vasomotor tone, but that after the blood pressure has fallen well below the critical level,[6] the vasoconstrictor center suffering from impaired blood supply becomes weakened, loses its tone, and as death approaches, the perfusion rate rises.

The last three experiments in table 2 were made on animals that had received spinocaine before they were bled. In these animals the

6. Cannon, W. B., and Cattell, McK.: Experimental Traumatic Shock; Critical Level in Falling Blood Pressure, Arch. Surg. **4**:300 (March) 1922.

perfusion rate was unchanged or increased by hemorrhage. The normal initial vasoconstrictor response to hemorrhage was absent. As this vasoconstrictor response is probably compensatory in nature, it becomes clear why experimental animals and patients under spinal anesthesia react so poorly to hemorrhage.[7] The normal subject is able to compensate, in part at least, for diminution in blood volume by active constriction of the arteries to the less vital organs. Such organs thereby suffer from a decreased blood supply,[8] but the blood pressure remains fairly well up, and circulation to the vital organs is maintained despite the marked diminution in cardiac output.[9] In subjects under spinal anesthesia, the power of active vasoconstriction is, however, more or less completely absent because of the paralysis of vasomotor fibers, and loss of a relatively small amount of blood is fatal.

COMMENT

It is believed that the studies reported in this paper may have a significance beyond the light they throw on the physiology of spinal anesthesia. Clinically, one observes two different kinds of traumatic shock which are confusing because they so often occur simultaneously. The more important and more serious of these is the so-called secondary shock, which occurs some minutes or some hours after injury. The recent researches of Blalock and his co-workers seem to show beyond question that local loss of blood plasma or of whole blood accounts in large measure for the phenomena observed in this type of shock, which is characterized by diminished blood volume, an early fall in cardiac output, a relatively late fall in mean arterial pressure and, presumably at least, by an initial and compensatory increase in vasomotor tone. The primary physiologic disturbance in this condition seems to be diminished blood volume.

Primary traumatic shock or collapse is quite different. It comes on immediately after injury and is presumably of reflex origin. The drop in blood pressure occurring immediately after a gunshot wound and that following trauma to the central nervous system presumably represent types of primary shock. The decrease in blood pressure in

7. Burch, J.; Harrison, T. R., and Blalock, A.: Comparison of the Effects of Hemorrhage in Dogs Under Ether and Under Spinal Anesthesia, Arch. Surg., in press.

8. Gesell, R.: Factors Controlling Volume-Flow of Blood, Am. J. Physiol. **47**:428, 1919.

9. Blalock, A.: Regulation of Circulation; Relative Importance of Nervous, Endocrine and Vascular Regulation in Response of Cardiac Output to Anoxemia, Am. J. Physiol. **83**:284, 1927.

subjects under spinal anesthesia appears to belong to this group. If so, primary shock is characterized by an initial decrease in vasomotor tone with an early drop in blood pressure and a relatively late decrease in cardiac output, the blood volume being unaffected. In order to classify our concepts, it might be well to speak of neurogenic (rather than primary) and hematogenic (rather than secondary) shock.

SUMMARY

A method for the study of arterial tone by reverse arterial perfusion has been described.

A normal animal responds to hemorrhage by an initial vasoconstriction.

After the blood pressure has fallen below 40 mm. vasodilatation occurs, and death soon follows.

Spinal anesthesia is usually followed by a marked vasodilatation. This may involve the unanesthetized as well as the anesthetized areas.

The constrictor response to hemorrhage is abolished by spinal anesthesia, and it is believed that this observation explains the unusual susceptibility to hemorrhage of patients and animals under spinal anesthesia.

The bearing of these observations on current conceptions of shock has been discussed, and the suggestion has been made that the terms neurogenic and hematogenic be substituted for primary and secondary shock, respectively.

THE EFFECT OF THE ADMINISTRATION OF FLUID ON THE FALL IN BLOOD PRESSURE CAUSED BY SPINAL ANESTHESIA*

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Our previous studies [1] have dealt with the physiologic changes in the circulation caused by spinal anesthesia. The present and subsequent studies are concerned with the treatment, and more particularly with the prevention, of the untoward effects. Of these effects, the fall in blood pressure is the most important, because it is the most common. In other types of low blood pressure the therapeutic value of large amounts of fluid is well recognized. Consequently, the effect of fluid has been studied first.

The methods employed have been discussed in some detail in the previous papers and need not be presented here. The amount of spinocaine (a proprietary procaine preparation) used varied from 0.5 to 2 cc., depending on the size of the dogs. All of the animals received barbital from one to two hours before the spinal puncture. The blood pressure was recorded from the carotid artery.

In table 1 are presented the observations on a series of dogs that received no fluid. The smallest percentage drop in blood pressure was 28; the greatest, 70, and the average, 41. Animals that had received small amounts, i. e., from 2 to 7 cc. per kilogram of body weight of physiologic solution of sodium chloride intravenously showed similar changes (table 2). In this group the smallest drop in mean arterial pressure was 27 per cent, the greatest, 70 per cent, and the average 42 per cent. One may therefore conclude that such small intravenous infusions are of no value in preventing the diminution in blood pressure.

However, when larger amounts of saline solution were given, a beneficial effect was noted (table 3). In this group of animals that

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* Submitted for publication, July 3, 1930.

* From the Departments of Gynecology and Medicine of Vanderbilt University.

1. Burch, J. C., and Harrison, T. R.: The Effect of Spinal Anesthesia on Arterial tone, Arch. Surg., this issue, p. 1040; Burch, J. C.; Harrison, T. R., and Blalock, A.: Comparison of the Effects of Hemorrhage under Ether Anesthesia and under Spinal Anesthesia, ibid. **21**:693 (Oct.) 1930; Burch, J. C., and Harrison, T. R.: Effect of Spinal Anesthesia on Cardiac Output, ibid. **21**:330 (Aug.) 1930.

received from 13 to 20 cc. of physiologic solution of sodium chloride per kilogram of body weight, the smallest decrease in blood pressure was 8 per cent, the greatest 27 per cent and the average 19 per cent.

TABLE 1.—*Control Experiment: The Effect of Spinocaine on the Blood Pressure of Dogs Receiving no Fluid*

Experiment Number	Amount of Fluid Administered, Cubic Centimeters per Kilogram	Mean Arterial Pressure Before Spinocaine, Millimeters of Mercury	Mean Arterial Pressure After Spinocaine, Millimeters of Mercury	Change in Mean Arterial Pressure, per Cent
3	0	84	60	—29
5	0	138	90	—31
7	0	108	66	—39
8	0	120	70	—42
10	0	100	66	—34
11	0	104	462	—58
12	0	116	84	—28
13	0	114	34	—70

Average arterial pressure before spinocaine, 110 mm. of mercury; after spinocaine, 65 mm.; average diminution in arterial pressure after spinocaine, 41 per cent.

TABLE 2.—*The Effect of Spinocaine on the Blood Pressure of Dogs Receiving Small Amounts of Solution of Sodium Chloride Intravenously*

Experiment Number	Amount of Fluid Administered, Cubic Centimeters per Kilogram	Mean Arterial Pressure Before Spinocaine, Millimeters of Mercury	Mean Arterial Pressure After Spinocaine, Millimeters of Mercury	Change in Mean Arterial Pressure, per Cent
33	2	108	32	—70
36	4	158	114	—28
45	6	95	70	—27
32	6	102	50	—51
34	7	90	60	—33

Average arterial pressure before spinocaine, 110 mm. of mercury; after spinocaine, 65 mm.; average diminution in arterial pressure after spinocaine, 42 per cent.

TABLE 3.—*The Effect of Spinocaine on the Blood Pressure of Dogs Receiving Large Amounts of Solution of Sodium Chloride Intravenously*

Experiment Number	Amount of Fluid Administered, Cubic Centimeters per Kilogram	Mean Arterial Pressure Before Spinocaine, Millimeters of Mercury	Mean Arterial Pressure After Spinocaine, Millimeters of Mercury	Change in Mean Arterial Pressure, per Cent
46	13	106	98	— 8
31	14	116	88	—24
44	14	98	82	—16
34	16	98	72	—20
29	20	140	102	—27

Average arterial pressure before spinocaine, 112 mm. of mercury; after spinocaine, 90 mm.; average diminution in arterial pressure after spinocaine, 19 per cent.

The experiments seem to show clearly that the administration of salt solution, intravenously, immediately prior to the induction of spinal anesthesia, may be of value in preventing the drop in blood pressure, provided sufficient salt solution is given. One liter should constitute an adequate amount for an adult patient of average size.

FORTY-FOURTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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(Concluded from p. 874)

MISCELLANEOUS

Injury of the Serratus Magnus Muscle.—Fitchet [45] reported five cases of injury of the serratus magnus muscle. A winged scapula and an ability to invaginate the overlying skin into the subscapular space, together with persistent pain, a drooping shoulder and an inability to elevate the arm above the right angle, were the signs on which the diagnosis had to be made. The prognosis was good with early treatment.

Gaucher's Disease.—The roentgenologic changes in the bones in Gaucher's disease were described by Kirklin and Hefke.[46] In the patient whom they had studied, changes were found in the long bones only. There was a generalized osteoporosis with thinned cortex similar to senile atrophy of the bone. There were also localized areas of destruction in the shafts of the long bones. The authors discussed the disturbance in lipoid metabolism with the liberation of kerasin which was taken up by cells of the reticulo-endothelial system. The atrophy and localized areas of destruction were due to the invasion of the bone marrow by these cells. A review of the literature was appended.

45. Fitchet, S. M.: New England J. Med. **203**:818, 1930.
46. Kirklin, B. R., and Hefke, H. W.: Am. J. Roentgenol. **24**:258, 1930.

Lesions of the Bone in Tardive Heredosyphilis.—Pendergrass, Gilman and Castleton [47] recorded a case of hereditary syphilis in which lesions of the bones became manifest during the third decade of life. No diagnosis had been made before this and no treatment had been given. In this case practically every known type of syphilitic lesion of the bone was present. There were increased density of the skull, osteomyelitis of the jaw, cystic degeneration of the upper end of the humerus, atrophic and hypertrophic changes at the elbow, gummas, destruction of cartilage at the hips and knees, coxa vara and effusion into the joints of both knees. Improvement followed antisyphilitic treatment.

Ganglion.—McEvedy [48] advocated the treatment of ganglions by injection. After aspirating the contents or expressing them through the needle, from 0.5 to 2 cc. of a 5 per cent solution of sodium morrhuate was injected into the ganglion. There was mild pain for a day or two. In two weeks the ganglion should have disappeared. McEvedy reported ten cases, eight of which were cured; the two failures being due, in his opinion, to too small a dose.

BONE, JOINT AND TENDON SURGERY

Pain in the Lower Part of the Back.—Campbell [49] stated that he had performed lumbosacral or sacro-iliac arthrodesis in 63 patients with the following conditions: infection, 35; trauma, 11; congenital anomalies, 3; benign tumors, 1, and tuberculosis, 13. For the lumbosacral fusion he utilized a curved graft removed from the posterior iliac crest, and for fusion of the sacro-iliac joint he employed an extra-articular operation performed by fusing adjacent portions of the sacrum and ilium and packing bone chips between them.

Technic of the Bony Shelf Operation in Congenital Dislocation of the Hip.—Soutter [50] suggested a method of creating a bony shelf over the head of the femur in patients with an old irreducible congenital dislocation of the hip and also in those with an extremely shallow acetabulum. The capsule of the joint, a portion of the ilium and the trochanter were exposed by an incision running from the anterosuperior portion of the spine to 2 cm. below the top of the trochanter and then backward and upward. A broad long slot was made through the outer and inner tables of the ilium just above the head of the femur, and a thick graft removed from the trochanter and upper portion of the shaft of the femur was placed horizontally in the slot. A square piece of

47. Pendergrass, E. P.; Gilman, R. L., and Castleton, K. B.: Am. J. Roentgenol. **24**:234, 1930.

48. McEvedy, P.: Lancet **2**:902 (Oct. 25) 1930.

49. Campbell, W. C.: Surg. Gynec. Obst. **51**:381, 1930.

50. Soutter, R.: Surg. Gynec. Obst. **51**:249, 1930.

bone cut from the outer table of the ilium above the acetabulum was lowered and brought into contact with the femoral graft, the lower edge being held with catgut stitches.

This procedure had been used successfully in 9 cases by Soutter during the last three years in patients ranging from 6 to 18 years of age.

[ED. NOTE.—The technic is neat and constructs a prop to prevent upward tilting of the bony shelf.]

Extra-Articular Arthrodesis of the Hip.—Mathieu [51] had performed extra-articular arthrodesis of the hip in 21 cases by the following technic: The patients were placed on an orthopedic table with the leg abducted. The Smith-Petersen incision was used. The greater trochanter was sectioned. A flap of the ilium was turned down so as to reach the cut edge of the trochanter. The freed trochanter was then slid on to the wing of the ilium and fixed with screws or nails. A plaster was applied for three months. The indications for the operation were: (1) painful forms of chronic arthritis, (2) unstable hips (3) hips incompletely ankylosed with progress toward deformity.

Operative Treatment of Lesions of the Lower Extremity in Diabetes Mellitus.—McKittrick and Pratt [52] reviewed 281 operations on the lower extremity in patients with diabetes mellitus. They found it helpful to divide the lesions into those due to arterial insufficiency and those due primarily to infection. *Staphylococcus albus* was the organism most frequently encountered in infections of the feet. Gas bacillus infection was present in a single case. In the cases of circulatory insufficiency not requiring amputation, the passive exercises of Buerger were found helpful in stimulating circulation. Spinal anesthesia was the preferred form. The authors discussed the indications and methods of drainage or amputation. The mortality in these cases was 16.6 per cent.

Surgery of the Knee Joint.—Henderson's [53] article was based on a review of 256 cases of injury to the semilunar cartilages in which operation was performed at the Mayo Clinic. There were 234 cases of injury to the internal semilunar cartilage and 22 of derangement of the external semilunar cartilage. End-results were obtained in 238 of the 256 patients; 77 per cent were relieved from all trouble, 14 per cent were improved and 9 per cent were not benefited. The results from removal of the internal semilunar cartilage were slightly better than those following excision of the external cartilage. In the series there were 42 cases in which the pathologic process demonstrated at the time of operation was not sufficient to account for the patient's symptoms; of 35 patients

51. Mathieu, P.: Presse méd. **38**:165, 1930.

52. McKittrick, L. S., and Pratt, T. C.: Operative Treatment of Lesions of the Lower Extremities in Diabetes Mellitus, Arch. Surg. **21**:555 (Oct.) 1930.

53. Henderson, M. S.: Surg. Gynec. Obst. **51**:720, 1930.

in this series, 13 were cured, 8 were improved and 14 were unimproved by the removal of one or the other cartilage. The diagnosis, operative technic and postoperative care were thoroughly discussed.

FRACTURES

Nonunion in Fractures.—Albee [54] stated that the chief causes of nonunion in fractures were: (1) failure of granulation tissue to bridge the gap; (2) a scar formed by granulation tissue before the osseus tissue had been established; (3) too early moblization; (4) rough manipulation of soft callus; (5) interference with circulation at the site of fracture; (6) infection; (7) steel plates; (8) absorption of solid callus before the restoration of trabecular alinement. He pointed out that fractures in elderly persons united almost as readily as those in younger adults, but that intra-uterine fractures were the most difficult to treat.

The methods of nonoperative treatment were discussed, such as diet, artificial light and various means of stimulating the fracture site locally, none of which had been wholly successful. Albee believed that there was only one successful way of treating nonunion of fractures, and that was by open operation and the massive bone graft. Motor driven instruments were considered essential, and absolute fixation of the part for a minimum of eight weeks was necessary. The graft was usually taken from the sound tibia although the sliding graft sometimes sufficed. Various types of graft and the method of fixation of the graft were discussed. A review of cases was appended.

Dorrance [55] said that osteoperiosteal grafts were indicated in selected cases of nonunion. He based his conclusion on observations, both clinical and experimental. The ideal conditions for successful results were: The osteoperiosteal graft should contain a good supply of bone with the periosteum. Periosteum that was stripped from the bone would not produce bone. One must be just as careful to fasten the graft to the bones as in the case of full thickness grafts. The same care must be used in preparing the bed for reception of the graft as in full thickness grafts. It required a longer time for the osteoperiosteal graft to become solid than for a full thickness graft. In all bone grafts one should secure as complete immobilization as possible during the first two months. The thickness and strength of the graft depended on the amount of weight-bearing that was to be required.

Fractures of the Cervical Vertebrae.— Le Fevre and Jackson [56] presented their method of fixation and support of the head in fractures

54. Albee, F. H.: Surg. Gynec. Obst. **51**:289, 1930.

55. Dorrance, G. M.: Ann. Surg. **92**:161, 1930.

56. Le Fevre, L., and Jackson, S.: Fixation and Support of the Head in Fracture of the Cervical Vertebrae, J. A. M. A. **95**:1669 (Nov. 29) 1930.

of the cervical vertebrae. The apparatus consisted of two hinged ovals of irons joined together with turnbuckles. The ovals were fitted, one to the curve of the body around the neck under the chin, and the other around the base of the neck and over the shoulders. The turnbuckles allowed for adjustments or traction.

Fractures of the Acetabulum.—Cubbins, Conley and Callahan [57] classified fractures of the acetabulum as follows: (1) fracture of the rim; (2) fractures involving one or two of the bones making up the acetabulum; (3) perforating fractures, and (4) extensive fractures involving all the bones making up the acetabular cup.

Treatment was based on the type of deformity. Longitudinal traction alone might suffice. If the head was centrally dislocated, a combination of lateral and longitudinal traction should be tried. A screw placed in the trochanter and into the neck was advocated as a means of gaining effective lateral traction. If the femoral head was centrally dislocated and locked, open operation offered the only hope for restoration of the normal joint.

Separation of the Lesser Femoral Trochanter.—Lapidus [58] reported 2 cases of separation of the lesser femoral trochanter, one with bony separation as shown by roentgenograms and the other with probably a partial rupture of the tendinous fibers of the iliopsoas muscle. These cases were rare, occurring mostly in boys between the ages of 13 and 17 as a result of sudden overexertion of the iliopsoas muscle, usually during running. The symptoms were pain and tenderness over the lesser trochanter and weakness or complete loss of flexion of the thigh. Treatment consisted of rest in bed with relaxation of the iliopsoas muscle by means of a plaster spica applied with the hip in flexion, external rotation and adduction. Complete recovery could usually be expected.

Fractures of the Femoral Neck.—Reggio [59] reporting study of patients with fractures of the neck of the femur treated at the Massachusetts General Hospital, said that he in no way attempted to voice an opinion in regard to the advantages of any form of treatment. He merely observed the end-results in consecutive cases in which closed methods had been used. No case had been omitted; thus all selection had been avoided. Forty-nine patients were treated by the Whitman method; 13 died, 18 showed good results, 5 fair results, 7 poor results, and in 6 the outcome was unknown. Twenty-one patients were treated by other methods; 5 died, 4 had good results, 2 fair results, 5 poor

57. Cubbins, W. R.; Conley, A. H., and Callahan, J. J.: Surg. Gynec. Obst. **51**:387, 1930.

58. Lapidus, P. W.: J. Bone & Joint Surg. **12**:548, 1930.

59. Reggio, A. W.: J. Bone & Joint Surg. **12**:819, 1930.

results, and in 5 the results were unknown. Therefore, "good" results were obtained in 60 per cent of the cases treated by the Whitman method, as against 36.4 per cent treated by other methods.

Santos [60] made a careful study of the changes in the femoral heads in 15 cases after complete intrascapular fracture of the neck of the femur. He found that the life of the proximal fragment depended on the circulation through the ligamentum teres. The vessels in the ligamentum teres were more abundant in young persons, but were adequate in many elderly persons. Bony union occurred in most cases in which the head remained alive, and there was adequate reduction and fixation. Even in the presence of necrosis of the proximal fragment, union might take place with efficient reduction or impaction followed by immobilization. Weight-bearing should be avoided until repair of the head is completed. The replacement of the dead bone took place by invasion of newly formed tissue from the round ligament and by vascularization through adhesions formed between the capsule and the eroded surface of the fracture. It was usually possible to determine from roentgenograms in from six to ten weeks whether the head was dead or alive. Where the head was alive it would show the same amount of atrophy during immobilization as the distal fragment. In case of necrosis of the head it would show greater density than the distal fragment, since it could not show bony atrophy if its blood supply were destroyed. When there is nonunion and necrosis of the femoral head, a reconstruction operation should be performed. Where there is nonunion and the head of the femur remains alive, the fixation of the fracture with a bone peg is indicated if the general condition of the patient is good.

[Ed. Note.—These observations made in Phemister's Clinic are worthy of serious consideration and offer a rational basis for the selection of proper methods of treatment in patients with delayed union of the femoral neck.]

Fractures of the Femoral Shaft.—Eve [61] stated that open reduction should be performed in fractures of the shaft of the femur only when conservative treatment failed. One-fourth contact of the ends of the fracture was sufficient, and many good functional results were observed when overriding was present. For the upper third of the femur the author preferred suspension and traction since most of the fractures in this region were oblique. He found that 70 per cent of the fractures in the middle third of the femur were transverse. Here he used a plaster spica cast in selected cases. The cast was shortened to the knee in three or four weeks. In the other fractures of the middle third of

60. Santos, J. V.: Changes in Head of Femur After Complete Intrascapular Fracture of Neck, Arch. Surg. **21**:470 (Sept.) 1930.

61. Eve, D.: South. M. J. **23**:813, 1930.

the femur he used traction with the posterior surface of the thigh well padded to prevent backward bowing at the site of fracture. In the lower third of the femur he found the backward displacement of the lower fragment the most difficult feature. Here he advised the use of skeletal traction with a pin through the femoral condyles and with the knee flexed almost to a right angle.

Fractures of the Patella.—Leavitt [62] suggested the use of free strips of fascia about 1½ to 2 inches (3.8 to 5 cm.) wide for fixation of the patellar fragments, these being attached to the quadriceps tendon for a distance of 1½ inches above the patella and also to the patellar tendon for the same distance below it. The edges were sutured to the tendon and the periosteum with interrupted fine plain catgut. The use of these wide and long strips of fascia gave a large area of adhesion and a consequent increase in strength.

This method was first used in 1926 in three patients who had been operated on before, and in whom the patella was again fractured. There had been no recurrences in these cases, and the patients operated on subsequent to 1926 had had no complications or setbacks.

Traction Apparatus for Naval Vessels.—Shaar [63] had made an addition to the usual overhead traction and suspension frame whereby jar and pendulum motion of the weights was prevented in hospital ships. This addition consisted of a steel tube through which the cords passed to the weights. The tube could be attached at any angle and at any height. Swaying of the weights was prevented.

DISLOCATIONS

Habitual Dislocation of the Shoulder.—Henderson [64] reported forty operations on 37 patients with habitual dislocation of the shoulder. Anterior capsulorrhaphy performed on 16 patients for anterior recurring dislocation resulted in cure in 37.5 per cent, all of these operations being done more than ten years before. Three patients who underwent posterior capsulorrhaphy for posterior dislocation remained well. Of 8 patients who underwent Claremont operations more than five years before, 50 per cent were cured. Tenosuspension performed on 10 patients had resulted in cure in 100 per cent of the cases: in 2 cases lasting for more than five years after operation, in 2 for more than three years, in 1 for more than two years, in 2 for more than one year, in 2 for more than eight months and in 1 for more than six months. The success of the operation of tenosuspension depended on the careful placing

62. Leavitt, P. H.: New England J. Med. **203**:728, 1930.

63. Shaar, C. M.: U. S. Nav. M. Bull. **28**:718, 1930.

64. Henderson, M. S.: Habitual Dislocation of the Shoulder, J. A. M. A. **95**:1653 (Nov. 29) 1930.

of the strong piece of the tendon of the peroneus longus muscle to act as a suspension ligament through drill holes in the acromion process and the head of the humerus. Small incisions were required, and this was an important consideration in women. The operation did not require opening of the capsule of the joint.

[Ed. Note.—Henderson's study has gone a long way toward solving the problem of habitual dislocation of the shoulder. Suspension with fascia is less strong than that with tendon. One of us has had recurrences following the use of fascia alone.]

Repair of Bone.—Phemister [65] stated that aseptic necrotic bone in continuity with living bone was gradually invaded and more or less completely replaced by new bone through the process of creeping substitution, unless it was too inaccessible and was broken down by traumatism. In Koehler's, Kienbock's and Legg-Perthes' disease there was marked fibroblastic and fixed tissue phagocytic reaction and, in rare cases, an infiltrative reaction which resulted in absorption of necrotic bone without bony replacement by creeping substitution except in occasional instances. New bone formed from surviving osteogenic elements replaced the absorptive tissues more or less completely in the course of time. Histologically, the majority of these lesions appeared to have something more back of them than a simple bland embolus or injury cutting off the circulation and producing aseptic necrosis.

From work based on the histologic study of a series of experimental fractures produced in rabbits Ham [66] made the following summary:

"The adult bone cell is distinguished from the osteogenic cell which is found lining the bone in the periosteum, the Haversian canals and the endosteum. The osteogenic bone cells proliferate and differentiate into bone and cartilage. The usual method of bone repair is through the agency of these specific osteogenic cells and not by the metaplasia of fibroblasts."

Two factors, the presence of a local deposit of calcium salt and a good blood supply, were of great importance in effecting the differentiation of the osteogenic cell into bone. Cartilage resulted from the growth of osteogenic cells in the absence of these two factors.

Reaction of the Joints to Foreign Bodies.—Moulonguet and Mihailesco [67] studied the fate of fragments of bone introduced into the synovial cavities of rabbits by pulverizing bone and injecting the powder into the joints. In five days many of the fragments were included in the synovial membrane. In ten days all were surrounded by synovial cells and excluded from the joint. There were many macrophages. Changes

65. Phemister, D. B.: J. Bone & Joint Surg. **12**:769, 1930.
66. Ham, A. W.: J. Bone & Joint Surg. **12**:827, 1930.
67. Moulonguet, P., and Mihailesco, G.: Presse méd. **38**:453, 1930.

could be seen in some of the bony fragments. It seemed apparent that the greater part of the fragments were destined to be completely destroyed by osteoclasis or osteolysis and to disappear without damage to the joint. However, when the fragments were introduced by arthrotomy, there was a constructive reaction about some of the fragments, leading to the formation of osteophytes.

Structure and Function of Articular Synovial Membranes.—Sigurdson [68] studied the structure and function of articular synovial membranes, using the joints of the guinea-pig, rabbit, cat, dog, human fetus and adult. His conclusions were:

1. The inner surface of articular capsules is not formed by a distinct membrane, but by connective tissue modified as the synovial surface is reached.

2. The superficial synovial cells are not uniform in size or shape, some being quite small and round, while others are large with branching processes.

3. Synovial villi vary greatly in size and shape, and are composed of connective tissue resembling the part of the capsule from which they arise.

4. An excellent demonstration of variation in cell outlines on the synovial surfaces of articular capsules can be obtained by the use of silver-impregnation methods. The intercellular substance is found to be abundant in contrast to that of the pleura and peritoneum; and the apparent cell outlines are much more irregular and do not resemble those of an endothelial or mesothelial layer.

5. The presence of "stomata" in articular capsules is not confirmed.

6. Carbon particles, when injected into knee joints of guinea-pigs, evoke an inflammatory exudate in the joint cavity most marked on the third day after injection. Some of these carbon particles are taken up by the lymphatic vessels and are deposited in the inguinal and lumbar nodes, while others are removed from the joint cavity by the action of phagocytic cells, some of which gain the lymphatic vessels, while others remain in the subsynovial connective tissue for an indefinite period.

7. Iron, in the form of ferric ammonium sulphate, disappears from the joint cavities within thirty minutes after injection by way of the lymphatics.

8. Iodine, in the form of lipiodol, diffuses slowly through the joint capsule, a period of at least four days being required for its complete removal as judged by skiagrams.

9. Immobilization of the tibio-tarsal joints in rabbits over fifty-three days produced no marked structural changes in the joint capsule, but the amount of synovial fluid was considerably less.

Synovial Fluid in Infections and Neuropathic Arthritis.—Shands [69] reported the changes in the synovial fluid in 123 cases of inflammation of the joints. In 105 cases of chronic infectious arthritis, bacteria were recovered from the synovial fluid in 38.1 per cent. These bacteria were chiefly nonhemolytic streptococci. The cell counts and the percentage of polymorphonuclear cells were higher in the joints in which positive

68. Sigurdson, L. A.: J. Bone & Joint Surg. **12**:603, 1930.

69. Shands, A. R.: South. M. J. **23**:818, 1930.

cultures were obtained. The average count of cells was 8,109 per cubic millimeter when cultures were obtained and 5,144 per cubic millimeter when cultures were not obtained. There were 4 cases of acute, gonorrheal arthritis in 3 of which the gonococcus was recovered. The cell counts in these cases were higher than in the group of infectious arthritis. There were 4 cases of traumatic synovitis in which the swelling of the joint appeared several days after injury. Bacteria were recovered in 2 of these cases. In these the average cell count was 8,200. The synovial fluid was examined in ten neuropathic joints. Organisms were obtained in 4 cases: in 3 cases *Streptococcus viridans* was recovered, and in the fourth case *Staphylococcus aureus*. The average cell count in these cases was 3,200 with 57.7 per cent polymorphonuclears.

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